Harvard Medicine

SPRING 2012

Space Savers

Medicine gets a boost when scientists reach for the stars

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SPRING 2012 | VOLUME 85 | NUMBER 2

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SIGHTSEEING: The 2009 *Atlantis* shuttle mission was the first ride into space for alumnus–astronaut Robert Satcher (shown here), a journey that included a walk outside the shuttle.

NASA IMAGE

COVER: MATTIAS PALUDI

Special Report: Space Savers

Features

Departments

From the Dean

THOUGHTS ON INNOVATION

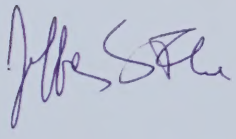
THE NIGHT SKY IS FILLED with mythic tales, including one tied to medicine, the story of Asclepius—healer, surgeon, and maker of restorative potions.

According to legend, Asclepius's study of the curative powers of plants began after he witnessed a snake revive itself by consuming a medicinal herb. With time, he became so adept at healing that Zeus struck him dead with a bolt of lightning. But, recognizing the good Asclepius had brought to humans, Zeus made him a god and assigned him a constellation, one known to the Greeks as the Serpent Bearer. Today, the symbol of the medical profession, a staff with a serpent coiled around it, recalls this legend.

Harvard Medicine takes us to the stars with this issue. For decades, HMS researchers have collaborated with the welter of skilled scientists who embody the nation's space enterprise. From leading space medicine research in the nascent NASA organization to serving as space-walking mission specialists today, HMS alumni have always made their mark. So too have researchers at the School. These Earth-based explorers have turned the challenges faced by space travelers, such as bone loss, depression, and circadian rhythm disruption, into research investigations. The results? Compounds that may delay osteoporosis, software that delivers behavioral therapy, and light therapy that can reset internal rhythms upset by jet travel or a trip to the moon.

If travel in the troposphere is more your speed, we invite you to read about the inroads technology is making on the delivery of medical care to remote regions of the earth. And if probing the creative and sometimes curious side of research scientists captures your fancy, our look at the quirky nature of gene naming may be just what you seek.

Speaking of searches, our nationwide effort to find a new editor for *Harvard Medicine* has been successful. With this issue, we enthusiastically welcome Ann Marie Menting. Formerly the magazine's associate editor, Ann Marie was the person on whom we relied as we—in tandem with our alumni leadership—searched for the magazine's new editor. She served up the Food issue and has now taken us to the stars. We eagerly anticipate the stories that will explore all points in between.



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Harvard Medicine is published three times a year at 25 Shattuck Street, Boston, MA 02115
Publishers: Harvard Medical School and Harvard Medical Alumni Association

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Email: harvardmedicine@hms.harvard.edu
Web: hms.harvard.edu/harvard-medicine
Third class postage paid at Boston, Massachusetts. Postmaster, send form 3579 to 107 Ave. Louis Pasteur, Boston, MA 02115
ISSN 2152-9957 · Printed in the U.S.A.

Letters to the Editor

SECOND OPINIONS FROM OUR READERS

Place Setting

I was impressed then by how remarkably engaged that and other classes of the late 1960s were in activities for the greater good.

TOM LLOYD
HERSHEY, PENNSYLVANIA

Blinkered Vision

I was thrilled to read the brief report, "Keen Edge," in the Winter 2012 issue of *Harvard Medicine*. I am an investigator and a clinician, and my area of specialization is glaucoma. Although most of my patients are elderly, I have been impressed that a significant number of them seem to exhibit increased cognitive abilities as they age.

In my field, it has been routine for physicians and patients to expect eyesight to diminish with age. And that, indeed, is a common phenomenon. The lens of the eye is an epithelial tissue that grows larger with age, and there is an inevitable optical deterioration associated with the development of cataract. But the advent of optically superb intraocular lenses has opened new vistas for cataract patients. In fact, it is routine for elderly individuals who have cataracts successfully extracted to see 20/20 or better, suggesting that aging alone does not result in deterioration of this tissue, which is, after all, part of the brain.

GEORGE L. SPAETH '58
PHILADELPHIA, PENNSYLVANIA

Apple Preserves

I read the article about Eric Chivian '68 and his work with heirloom apples in the Winter 2012 issue of *Harvard Medicine* with great interest. I attended lectures with him and his HMS classmates; I entered the Division of Medical Sciences as a graduate student in 1964 and graduated in 1970 with a PhD in pharmacology.

Dr. Chivian and I have both sought to preserve varieties of heirloom apples. In 1976, I founded Preservation Apple Tree Company. This avocational venture continued for 12 years and produced thousands of heirloom apple trees on dwarfing rootstock that have been planted throughout the United States. The company never turned a profit, however, so I turned over the idea—and the cultivars—to Pennsylvania-based Boyer Nursery, which had supported my venture. That nursery continues to produce nearly all of the heirloom varieties for which I had found budwood.

Your article caused me to reflect not only on my heirloom apple venture, but also on my days with the HMS Class of 1968. I was impressed then by how remarkably engaged that and other classes of the late 1960s were in activities for the greater good. It is nice to read that idealism remains alive and well, flourishing in at least one orchard.

TOM LLOYD
HERSHEY, PENNSYLVANIA

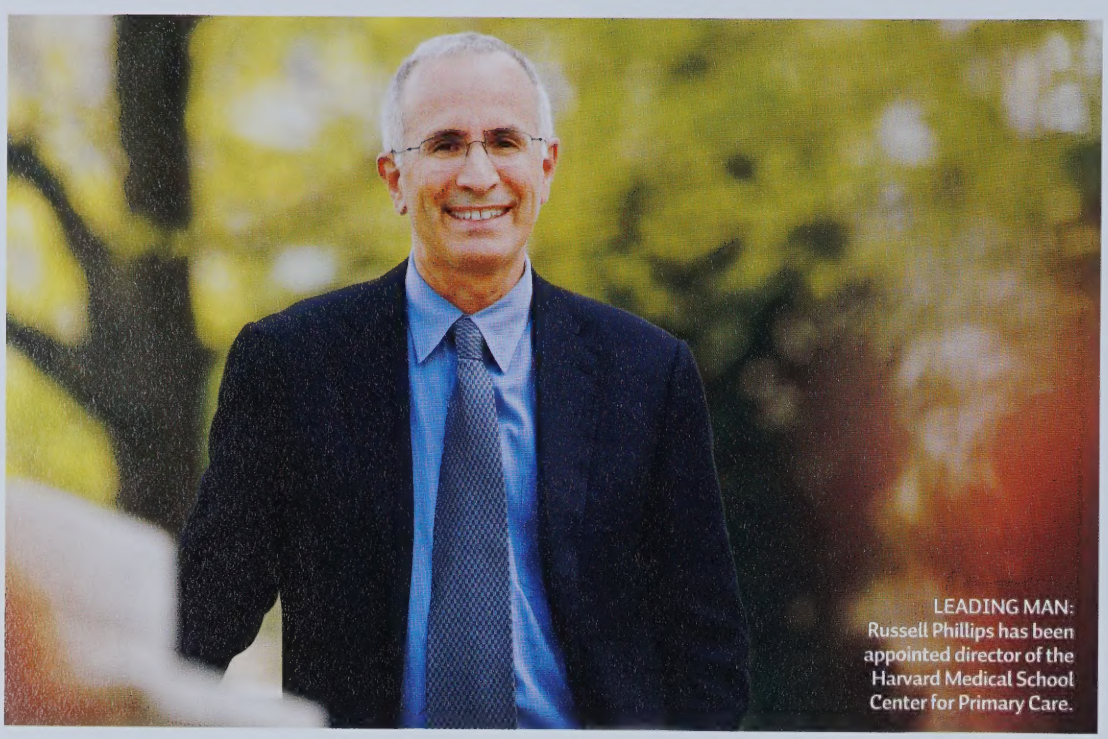
A Role for Fat

The article "Plate Shifts" in the Winter 2012 issue of *Harvard Medicine* reports that caloric intake still governs weight gain and loss. But does it really? In the same article, Walter Willett says, "There are a lot of strong beliefs in the area of nutrition—it's not unlike religion. The trouble is that the strength of these beliefs often seems to be inversely related to the strength of the data."

I finished HMS accepting as axiomatic the idea that caloric intake governed weight gain and loss; I accepted this with the strength of a religious conviction. It took years of contrary patient reports and my own observations before I realized this was an assumption. My clinical observations, instead, support the notion that body fat comes and goes with changes in the toxic load. I now consider any increase in body fat (no matter how great) to be, at least in part, a healthy response that might actually protect us from the toxins that otherwise would lead to more diabetes, heart disease, and high blood pressure.

KARL E. HUMISTON, '55
SAN DIEGO, CALIFORNIA

Harvard Medicine *welcomes letters to the editor. Please send letters by mail (*Harvard Medicine, *107 Avenue Louis Pasteur, Suite 111, Boston, Massachusetts 02115); fax (617-432-0446); or email (harvardmedicine@hms.harvard.edu). Letters may be edited for length or clarity. The magazine also welcomes ongoing feedback through its Readers' Panel. To learn more, write us at harvardmedicine@hms.harvard.edu.*



LEADING MAN: Russell Phillips has been appointed director of the Harvard Medical School Center for Primary Care.

JOHN SOARES

Prime Director

Leader selected for School's Center for Primary Care

The Harvard Medical School Center for Primary Care has announced inaugural leadership. Russell Phillips, who, together with Andrew Ellner '04 and David Bates, had been guiding the Center, has been appointed the Center's director, said Jeffrey Flier, dean of the faculty of medicine. The Center was made possible by a $30 million gift from an anonymous donor. Ellner, an HMS instructor in medicine, has been appointed codirector.

Phillips is an HMS professor of medicine and chief of the Division of General Medicine and Primary Care at Beth Israel Deaconess Medical Center. Ellner heads the School's Program in Global Primary Care and Social Change and is assistant medical director of the Phyllis Jen Center for Primary Care at Brigham and Women's Hospital. Bates, an HMS professor of medicine and chief of the Brigham's Division of General Internal Medicine, will remain involved as an advisor.

Phillips, Ellner, and Bates had central roles in the Center's creation and have been active in several programs already implemented, such as the Academic Innovations Collaborative, a $10-million initiative launched in early March. This collaborative aims to transform Harvard-affiliated primary care teaching practices to benefit more than a quarter million current patients.

Phillips is a recognized national thought leader in primary care, a reputation gained in part from his work as coleader of a BIDMC task force to improve transitions in care and reduce readmissions, and from his leadership in addressing effective care management for high-risk patients. The author of more than 200 publications, Phillips has written on disparities in care, patient safety, end-of-life care, screening for infection in office practice, and interventions to improve care for patients with chronic disease.

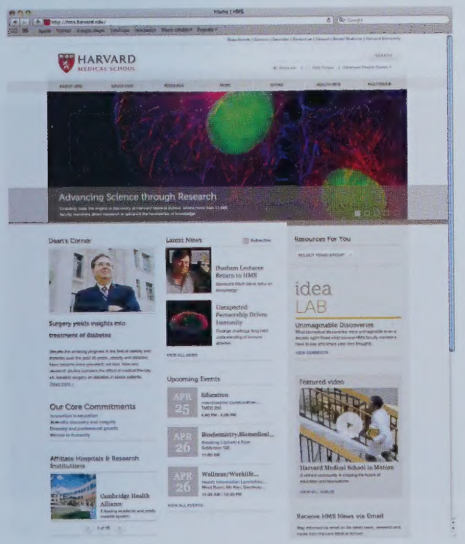
As a champion for global health, Ellner's passion for improving health systems for the most vulnerable populations around the world led him to serve as the clinical policy director of the Clinton HIV/AIDS Initiative's Rural Initiative and to manage the academic consortium of the World Health Organization's maximizing positive synergies initiative. Within the Center for Primary Care, Ellner coleads the Innovation Fellows Program, which is creating a community of leading primary care systems innovators at HMS.

"I look forward to working with all my colleagues and partners in fulfilling many of the Center's goals," said Phillips, "such as making primary care careers more desirable, and improving education so that primary care doctors are prepared to practice effectively in teams, to take responsibility for population health, to coordinate the care of patients with complex needs, and to engage and empower our patients."

—David Cameron

A Site for Sore Eyes

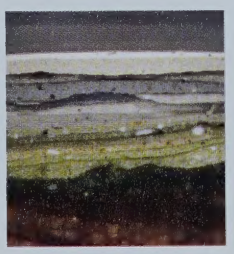
A redesigned and re-imagined HMS website launched in late March, ushering in a new cyber era for the School's community near and far. The site provides interactive opportunities that make the visitor's experience more inviting and engaging: the Dean's blog, comment sections for all content, a sign-up for topic-specific e-letters; a Google-based search tool; and a multimedia section rich with podcasts, videos, photo galleries, and social media links. Visit hms.harvard.edu and immerse yourself in HMS.



PAST AND PRESENT TINTS

Stay? Go? When it comes to green, Gordon Hall does both.

A FACELIFT IS IN THE WORKS for Gordon Hall. In the coming months, the Quad's first building will receive new windows that, in a nod to its past and present lives, both preserve the structure's historic integrity and improve its energy efficiency. Working with the Boston Landmarks Commission, HMS has devised a plan to replace the windows with ones that will reprise the look of those used 106 years ago.



The framework of the new windows will be darker than it is now, reverting to the original gray-green. Rick Shea, HMS associate dean for campus planning and facilities, hired a conservation firm to investigate the initial hues of the sashes, casings, and mullions.

"Gordon Hall's exterior," according to the firm's study, "retains a significant paint history on several elements. . . . Though it is a fairly common practice to remove previous paint . . . it appears that Gordon Hall's window finishes escaped this aggressive treatment resulting in a complete series of 16+ layers of exterior finishes on the wood window casings."

Although southern yellow pine, the wood used for the original windows, is no longer commercially available, it has for the most part withstood the ravages of time. Frames that need restoration will be repaired with mahogany. Locks and other hardware are also being replaced.

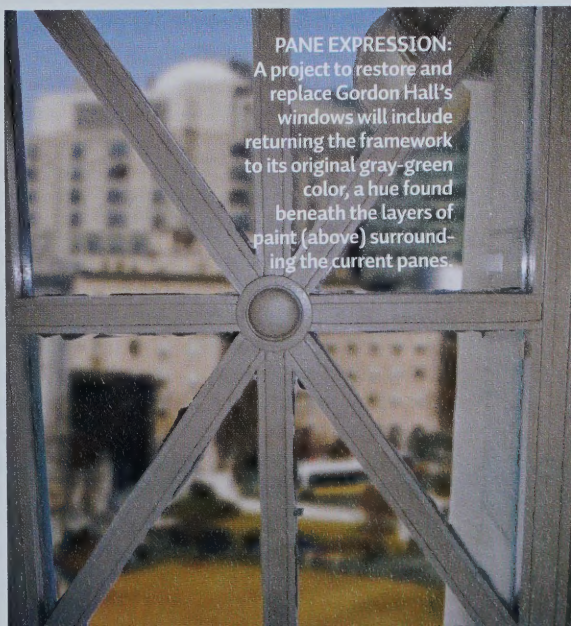
Amy Finstein, an instructor at the Massachusetts College of Art and Design, who served as an architectural historian on the project, says that changing the colors and styles of the windows would do more than alter the Quad's appearance, it would disrupt the integrity of one of the city's significant historical sites.

"Gordon Hall's windows," says Finstein, "are an important part of the building's classical aesthetic, with geometric patterns and symmetry that reinforce the architectural style of the entire HMS design. The medical school quad brought classical elegance and formal organization to an undeveloped area of Boston, echoing the larger national interest in the City Beautiful Movement."

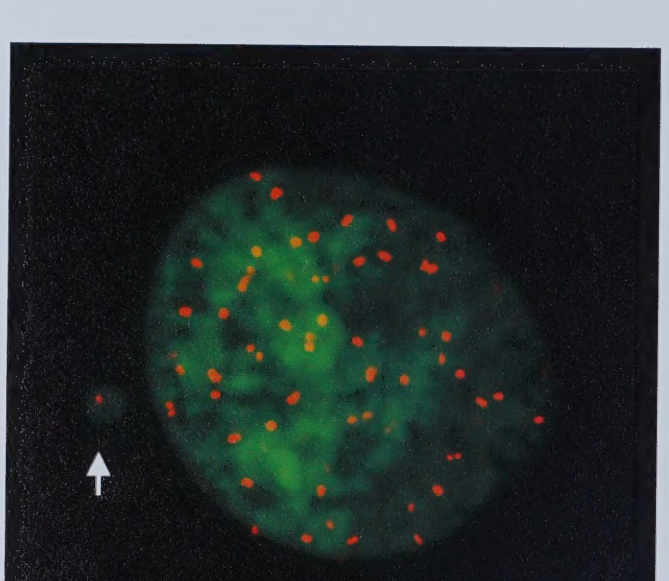
An architectural trend of the late nineteenth and early twentieth centuries, the City Beautiful Movement paid homage to Greek architecture and the ideals associated with it: social engagement, civic pride, democracy, philosophy, and modern medicine. It also focused on organizing spaces, transforming previously chaotic ill-kept cities into destinations that reflected order, cleanliness, and beauty. The Boston Public Library is a consummate example of this movement in the way it organizes Copley Square. A subset of this effort, Campus Beautiful, treated the campus as a city with very strongly organized spaces. It involved a host of schools, including HMS.

Gordon Hall's window restoration should be completed by November 2012.

—Valerie Wencis



PANE EXPRESSION: A project to restore and replace Gordon Hall's windows will include returning the framework to its original gray-green color, a hue found beneath the layers of paint (above) surrounding the current panes.



A BAD CRUSH

"Pulverized" chromosomes may trigger cancer

THEY ARE THE ROBINSON CRUSOES of the intracellular world: lone chromosomes, each marooned in its own "micronucleus" outside the nucleus, and often in cancer cells. In a paper published February 2 in *Nature*, HMS researchers describe how these micronuclei disrupt the chromosomes within them and produce cancer-causing gene mutations. The findings may point to a vulnerability in cancer cells that could be attacked by new therapies.

"The most common genetic change in cancer is the presence of an incorrect number of intact chromosomes within cancer cells, a condition known as aneuploidy," says senior author David Pellman, an HMS professor of cell biology and the Margaret M. Dyson Professor of Pediatric Oncology at Dana–Farber Cancer Institute. "Our study shows how aneuploidy—and specifically 'exiled' chromosomes—could lead to cancer-causing mutations and has implications for cancer prevention and treatment."

Pellman's team found that a chromosome in a micronucleus undergoes inefficient duplication that is out of sync with that of the cell's other chromosomes. This double whammy damages the chromosome, causing a degree of breakage that has been found in cancer cells generated from cells with micronuclei.

The team also found that these chromosomes appeared to be smashed to bits, a condition that linked the findings to those from studies that describe a phenomenon called chromothripsis. In cancer cells exhibiting chromothripsis, one chromosome of the cell shows massive amounts of breakage and rearrangement, while the remainder of the cell's genome stays largely intact. In addition, the team found that a third of the time, these pulverized bits are neither discarded nor digested by the cell. Instead they are donated to one of the daughter cells during cell division. The damaged chromosomes, therefore, could be incorporated into the cell's genome and initiate potential cancer-causing mutations.

Muscle Bound

Complex strabismus procedure offers faster recovery

SURGERY TO CORRECT THE EYE misalignment characteristic of strabismus can require operations on several muscles, causing lengthy recovery. In addition, the correction sometimes overcompensates for the problem, requiring repeat operations. A single simplified procedure adopted at Children's Hospital Boston has shown good results, researchers report, and allows for eye position to be fine-tuned in the recovery room or up to a week later, often avoiding follow-up surgery.

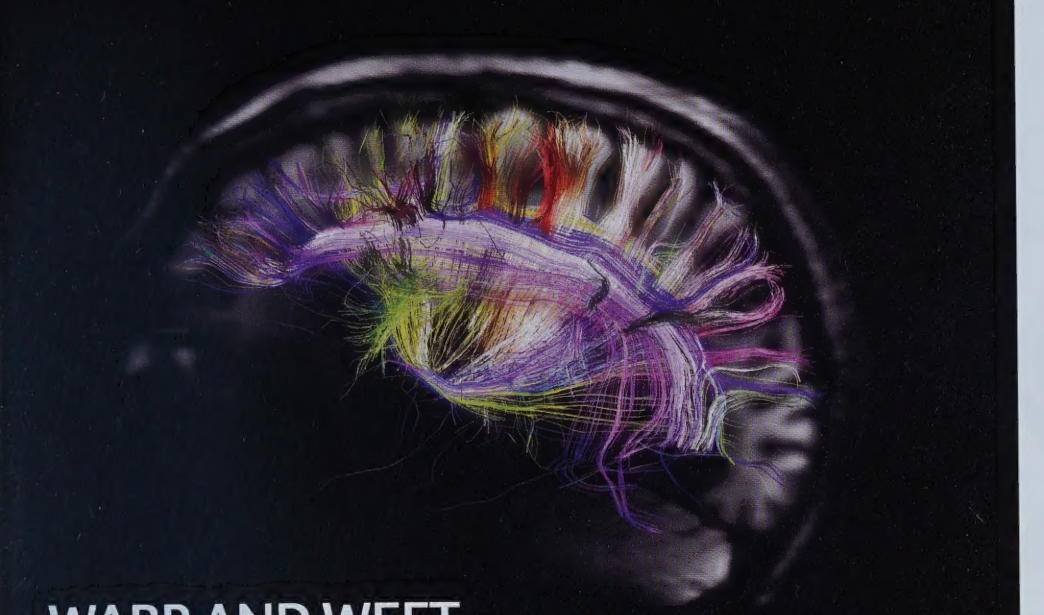
In the February issue of *Archives of Ophthalmology*, a team led by David Hunter, an HMS professor of ophthalmology and chief of ophthalmology at Children's Hospital Boston, reports on results of a procedure known as superior rectus transposition with adjustable medial rectus recession in 17 patients who could not move an eye outward. The new procedure enabled outward eye movement by repositioning a muscle that normally moves the eye up.

Unlike earlier procedures, the new one adjusts a single muscle, the superior rectus, to rotate the eye into place. In some cases, the medial rectus muscle is also adjusted, but the inferior rectus, often the source of complications, is untouched. The technique also uses an adjustable sliding "noose" knot to pull the eye muscles. The knot can be tightened or loosened afterward to adjust the eye's position in the recovery room or up to a week after surgery.

"Because we cannot always guarantee optimal alignment after surgery," says coauthor Linda Dagi '82, an HMS assistant professor of ophthalmology and director of Children's program for adults with strabismus, "we found the adjustable suture technique to be the best option for patients."

In their study, the team reviewed long-term outcomes and found improvements in horizontal eye movement and outward movement, with minimal cost to inward movement. Eight of the patients regained depth perception. No patient developed a significant problem with vertical eye alignment, a potential risk of the procedure.

NEIL GANEM AND KAREN CRASTA



WARP AND WEFT

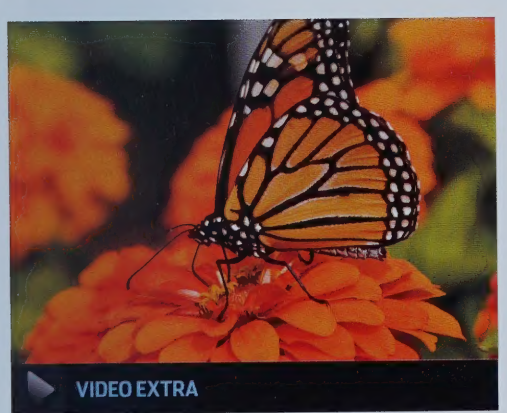
Complexity of primate brain rests on simple structure

HOW DO YOU BUILD A BRAIN? According to nature, you start with a curved, three-dimensional grid that's simple and orderly, say HMS researchers at the Martinos Center for Biomedical Imaging at Massachusetts General Hospital.

In the March 30 issue of *Science*, lead author Van Wedeen, an HMS associate professor of radiology and a member of the faculty of Harvard–MIT Health Sciences and Technology, reports his team's discovery of a remarkably simple organizational structure in the brains of humans and other primates. Employing sophisticated mathematical analyses of advanced imaging data, they found that the pathways carrying neural signals through the brain are built from parallel and perpendicular fibers that cross each other in an orderly fashion. The finding, says Wedeen, was completely unexpected.

"Although our findings could be described as a new longitude and latitude for the brain," he adds, "they're also leading us to an entirely new understanding of how and why the brain is organized the way it is. A simple grid structure makes both evolutionary and developmental sense. It's easier for a simple structure to change and adapt, whether we're talking about changes from evolution or from changes that can occur during an individual's lifetime—both the normal neuroplasticity associated with development and learning or the damage that results from injury or disease."

—Sue McGreevey



View the video at:
hms.harvard.edu/content/animal-magnetism-0

Research to Watch

Animal Magnetism

Using the tools of synthetic biology, researchers from HMS and the Wyss Institute for Biologically Inspired Engineering at Harvard University have induced magnetism in a non-magnetic organism: yeast. Because the researchers used a common cell pathway, their findings, reported February 28 in *PLoS Biology*, suggest that such magnetism could be achieved in cells used for a variety of industrial, medical, and research applications.

Saving the Good Guys

Antibody tool could aid efforts to treat, diagnose Alzheimer's

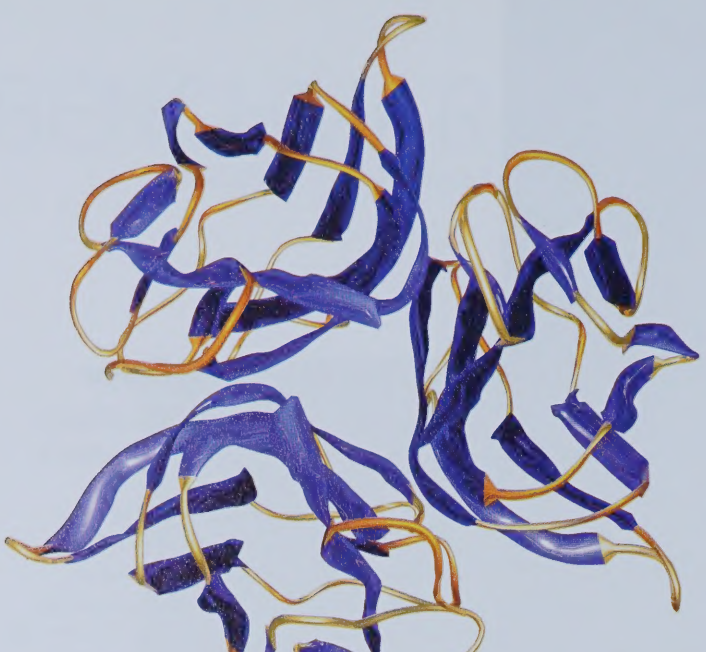
UNDER NORMAL CIRCUMSTANCES, the tau protein is a hard-working participant in memory and brain functioning. But in Alzheimer's and other neurodegenerative diseases, tau ceases to play a productive role in brain health and instead transforms to become a misshapen destroyer of brain cells.

Until now, distinguishing between the Jekyll and Hyde forms of tau has been challenging. But a new antibody technology developed by an HMS research team at Beth Israel Deaconess Medical Center can differentiate between the healthy tau isoform and the disease-causing one. In addition, it has demonstrated that only the disease-causing isoform is found in the neurons of Alzheimer's patients and that it is exhibited at a very early stage of disease. Described in *Cell*'s March 30 issue, the findings raise the intriguing possibility that antibodies and vaccines developed to target only the disease-causing tau isoform might be used to diagnose, treat, and potentially even prevent Alzheimer's.

"Since Alzheimer's disease takes at least a decade to develop, the major challenge to halt memory loss is to identify the initial period when the tau protein is transformed from 'good guy' to 'bad guy,'" says co-senior author Kun Ping Lu, an HMS professor of medicine and an investigator in Beth Israel's hematology and oncology division. "We have uncovered a new strategy to specifically remove disease-causing tau, while leaving healthy tau intact to carry out its important responsibilities."

Alzheimer's affects 5.4 million people in the United States and more than 30 million people worldwide. As the baby-boom generation ages and life expectancies continue to increase, these numbers are expected to rise dramatically, with some estimates projecting that by 2050 Alzheimer's will affect 120 million people worldwide. There is currently no effective treatment for the disease.

—Bonnie Prescott



Risk of Failure

Markers predict diabetes-linked loss of kidney function

AN ACCURATE PREDICTOR of renal failure risk in patients with type 1 and type 2 diabetes has been discovered by HMS researchers at Joslin Diabetes Center. The predictive elements: elevated levels in the bloodstream of tumor necrosis factor receptors 1 and 2 (TNFR-1 and TNFR-2).

In two studies published March 1 in the *Journal of the American Society of Nephrology*, the Joslin researchers report that high concentrations of TNFR-1 and TNFR-2 can accurately predict this risk ten years in advance. Currently available clinical tests cannot identify people at risk with that level of accuracy.

Says lead author Monika A. Niewczas, an HMS instructor in medicine, "High levels of these markers multiply the risk of developing kidney complications by three to five times." Niewczas is also a research associate in the laboratory of senior author Andrzej Krolewski, an HMS associate professor of medicine and head of Joslin's Section on Genetics and Epidemiology.

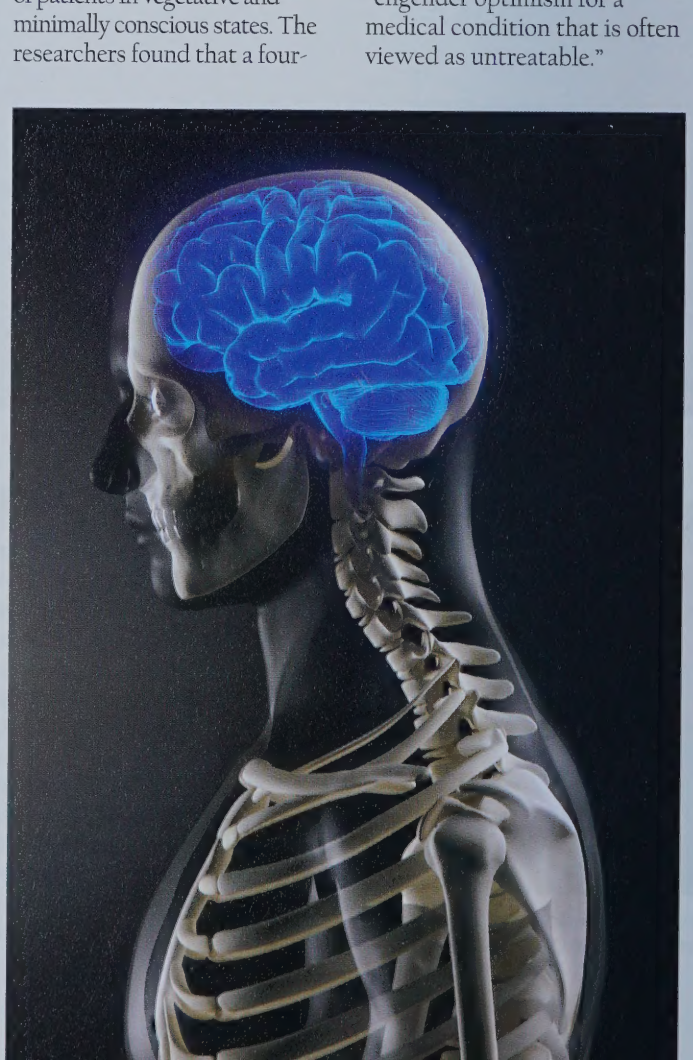
Tumor necrosis factors are proteins involved in inflammation, and a growing body of evidence indicates that certain inflammatory mechanisms together with high blood sugar contribute to renal injury in diabetes. This study showed that elevated levels of TNFR-1 and TNFR-2 led to renal disease in diabetic patients, regardless of the presence or absence of other clinical characteristics, such as blood pressure, albuminuria (a leak of large amounts of albumin into urine), and glycated hemoglobin, that are considered important risk factors for diabetic nephropathy.

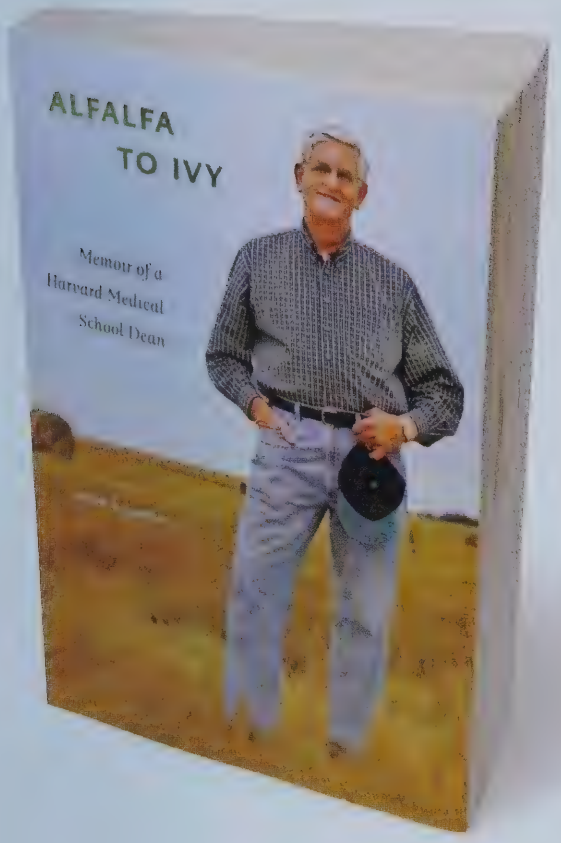
Renal complications, also known as diabetic nephropathy, are one of the most life-threatening complications of diabetes. Over time, this damage frequently leads to end-stage renal disease, when the kidneys can no longer work at the level needed to support everyday life. About a half million people in the United States have end-stage renal disease, and nearly 44 percent of these cases result from diabetes.

TRAUMA CARE

THE INFLUENZA MEDICATION amantadine hydrochloride may speed the pace of functional recovery for patients with post-traumatic disorders of consciousness. The finding, reported by HMS researchers at Spaulding Rehabilitation Hospital in the March 1 issue of the *New England Journal of Medicine*, comes out of a multinational study aimed at improving the treatment of patients in vegetative and minimally conscious states. The researchers found that a four-week regimen of amantadine administered within four months of traumatic brain injury prompted these patients to recover at significantly faster rates than patients administered a placebo.

Study leader Joseph Giacino, an HMS associate professor of physical medicine and rehabilitation and director of rehabilitation neuropsychology at Spaulding, says the results "engender optimism for a medical condition that is often viewed as untreatable."





FIELD DAY

Alfalfa to Ivy: Memoir of a Harvard Medical School Dean by Joseph B. Martin
(GUTTERIDGE BOOKS, 2011)
reviewed by Elissa Ely

IT'S A HARVARD DILEMMA: a person of uncountable accomplishments decides to write an autobiography. It's easy to be precise (as well as being a stellar clinician, the writer is also a renowned researcher). But is it so easy to be likeable?

There is a solution—but don't try it, because it's just been used. This autobiography has a cover photo of the author standing in a field of hay, wearing blue jeans, and holding a baseball cap. *Alfalfa to Ivy: Memoir of a Harvard Medical School Dean*, by Joseph B. Martin, is 397 pages of eminence. Yet in the end, that friendly alfalfa sets the tone.

In some ways, this is the story of a man who cannot stay put. Martin begins his book in the 1600s, with a set of maps and a history of the Swiss Anabaptists who became his Mennonite ancestors. Family life in Duchess, Alberta, Canada—population less than 100—included driving a tractor at five, going to church twice on Sundays ("I was a pious young man"), and skinning weasels. His early ambition was to become a missionary doctor. Instead, he became chief of neurology at Massachusetts General Hospital, co-editor of *Harrison's Principles of Internal Medicine*, co-creator of the Huntington Disease Center Without Walls, which mapped the gene for that disease, and dean of the medical school at the University of California, San Francisco, and at Harvard. He and his wife moved ten times before he finished his PhD, and their four children were born in four different cities. Martin may be a genius, but his wife is a saint.

All this might lead to a long resume under the cover of a book. Curiosity saves the author, though. He likes digging around, whether in soil, memory, cultural history, or genetics. He never forgets a name or event, either. This may have to do with a synesthetic gift he discovered while in medical school at the University of Alberta; he could organize numbers and dates in space, and—lucky student—memorized *Gray's Anatomy* in 3D. All this led to careers in neurology and neuroendocrine research, and they led to a full professorship at McGill University by age 37.

While at Massachusetts General Hospital, Martin discovered another gift: He could survive, better than most, "the internecine and often unforgiving warfare that...characterizes our academic institutions." He put his Mennonite tolerance to use as an administrator, and in 1989, became dean of UCSF, moving to San Francisco just in time for a 7.3 Richter-scale earthquake. In 1997, he came back to Harvard.

From the "adminosphere," Martin updated information technology, increased faculty and student diversity, renovated the Francis A. Countway Library of Medicine, negotiated contentious research hospital mergers, and, with unabashed symbolism, unlocked the front entrance to Building A for the first time in decades. *Open, ye mysterious administrative door!* He also pondered the paradox of Harvard, where hospitals that carry its prestigious name are not owned (and therefore can't be bossed around by) the medical school. "In sharp contrast to the symbolism of the job," he writes, "is the relative impotency that comes with it."

Always, he believed in "the imperative of collaborative relationships," and the power of listening, "the will to...try to understand what others are saying, even when it lacks clarity." After retiring in 2007, he returned to teaching. He also returned, a visitor, to the farm town where family still lives. It must have been during one of those visits that he returned to the family farm and the field of hay. Standing in its midst, he looks happy and humble—really, not like a dean at all.

Elissa Ely '88 is a psychiatrist at the Massachusetts Mental Health Center.

Savers

For more than five decades, humans have been hurtled into space. These pioneers have not only carried along all of life's necessities, they also have stowed carefully the power of imagination and the desire to discover. It is these intangibles that have built the legacy of space-based research. ■ We talked with some HMS researchers who, together with intrepid astronauts, have used the special laboratory of space to test the limits of their questions of science. Their stories provide a glimpse of the medical benefits these research collaborations have produced: pocket-sized imaging tools; light therapy to reset circadian clocks; drugs to rebuild bone; software-based behavioral therapy. And they provide a glimmer of what discoveries await.

NASA/MATTIAS PALUDI

Star Guide

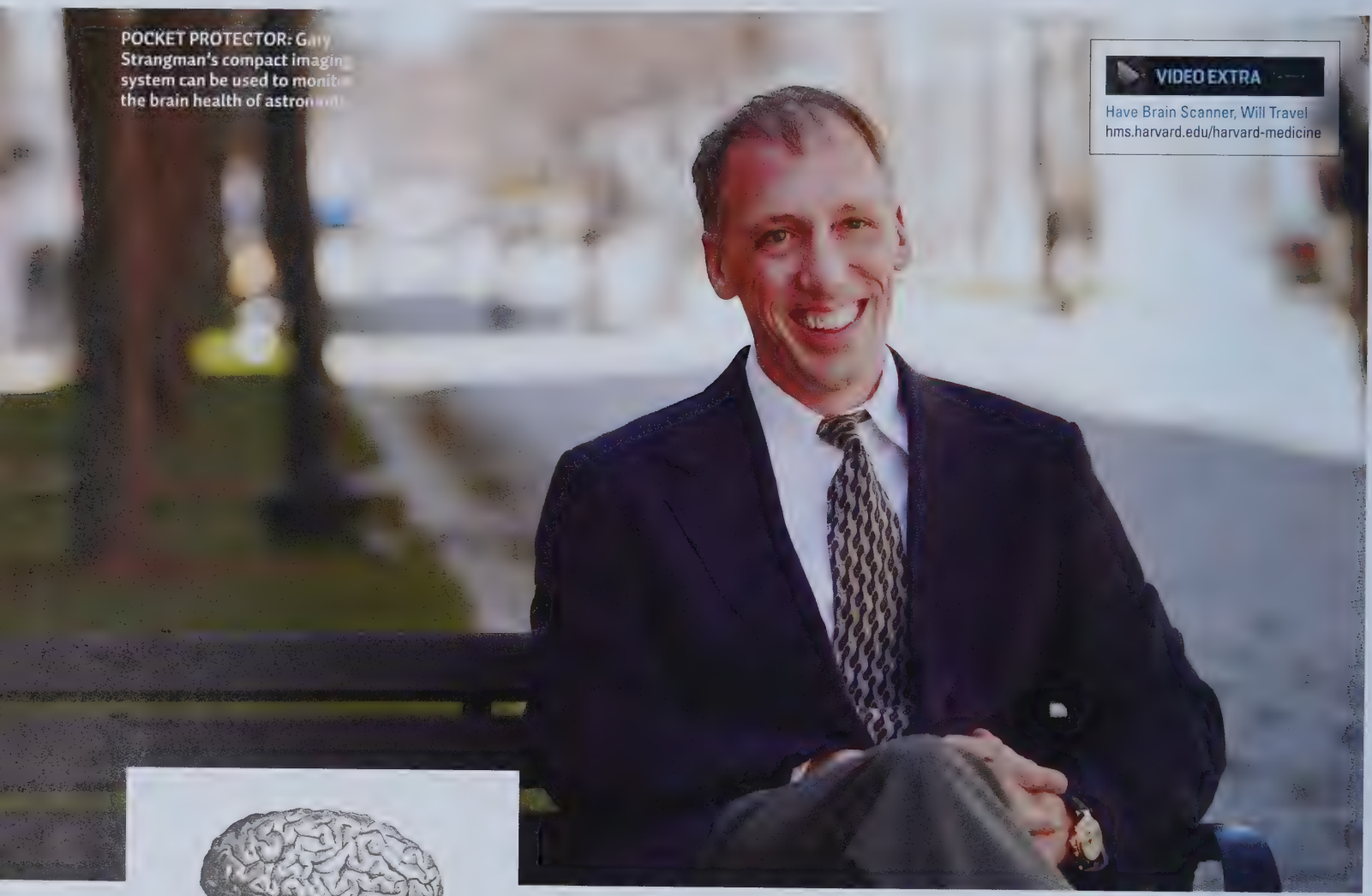
Biomedicine reaps rewards from scientific pursuits in space by Jake Miller

Inside Information

A pocket-sized system is taking near-infrared imaging to new heights

TRY AS YOU MIGHT, there's no way you can cram an MRI onto a spacecraft, not if you want to get it off the ground. But bringing such a device along would help determine what happens to astronauts' brains beyond Earth's atmosphere. Space, after all, is not a friendly place for the human brain: low-grade radiation bombards it, and hypoxia or hypercarbia can occur if equipment that generates oxygen or removes carbon dioxide in a spacecraft's tight confines isn't tweaked correctly.

All of these assaults change the brain's physical properties in ways that can be measured with neuroimaging tools. But if unwieldy instruments such as MRIs can't make the trip, what might fill the imaging void? Gary Strangman and his team of investigators think they have the answer: a near-infrared



POCKET PROTECTOR: Gary Strangman's compact imaging system can be used to monitor the brain health of astronauts

VIDEO EXTRA
Have Brain Scanner, Will Travel
hms.harvard.edu/harvard-medicine

Getting a clear picture of this area, the outermost cortex, is critical to determining the vitality of the higher order cognitive processes essential to sound decision making.

neuroimaging system, known as NIN. Compact and easy to use, NIN was developed for use not only in the isolation of space but also in the oxygen-thin heights of mountains and the injury-thick sidelines of sporting events.

Strangman, an HMS assistant professor of psychology and a neuroimaging researcher who directs the Neural Systems Group in the Department of Psychiatry at Massachusetts General Hospital, has developed the pocket-sized imaging system, which will allow astronauts to monitor their brain health while aloft. NIN can assess brain activity, edema, and oxygenation in the outermost inch of the brain at sensitivities that rival those of fMRI. Getting a clear picture of this area, the outermost cortex, is critical to determining the vitality of the higher order cognitive processes essential to sound decision making.

NIN measures the brain's relative health by picking up the absorption spectra of near-infrared light sent into the head by a pair of lasers. Based on these measures, NIN identifies areas of oxygenated and deoxygenated blood in the brain as well as concentrations of fluid from edema. The team is now testing whether the device is ready for the rigors of space.

Although NIN will never replace the deep imaging and exquisite spatial detail of a full-scale MRI scan, the handheld device could be a useful tool for health care professionals working in remote communities, at sporting events, and on the frontlines of civilian and military emergency medicine, Strangman says. His team is also testing NIN at high altitudes to learn more about the physiology of acute mountain sickness, a debilitating malady linked with the cognitive confusion and respiratory distress experienced by people unaccustomed to high altitudes, a group that includes U.S. soldiers deployed in the mountains of Afghanistan.

Architectural Detail

Clues to bone loss are found in space

Medical research has also sought to prevent bone loss in patients immobilized by stroke or spinal-cord injury, or in children with cerebral palsy or muscular dystrophy.

Bones are not the static, solid organs they seem. Exposed to stress from gravity or exercise, they grow bigger and stronger. Removed from such weighty obligations, they wither and weaken. For personnel on the International Space Station, this latter response is a constant worry: on average, space-traveling astronauts lose bone mass at the rate of 1 percent a month. That's ten times faster than the rate of bone loss among postmenopausal women.

"Without mechanical loading on the bones," says Mary Bouxsein, an HMS assistant professor of orthopedic surgery and a faculty member of the bioastronautics program in the Harvard–MIT Division of Health Sciences and Technology, "biochemical changes that signal bone loss can be found in the blood in just a couple of weeks."

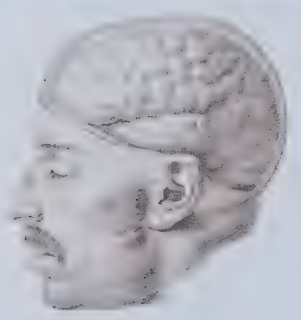
Actual loss follows quickly, and long missions increase the risk. If a year on the space station can jeopardize the structural integrity of an astronaut's skeleton, imagine the difficulties a three-year round trip to Mars could present to a space explorer.

For decades, NASA has been investigating ways to stem bone loss among astronauts. Medical research has also sought a means to prevent such loss in patients immobilized by stroke or spinal-cord injury, or in children with cerebral palsy or muscular dystrophy. Now, NASA–funded work by Bouxsein and colleagues at the University of North Carolina and the University of Colorado in Boulder, in collaboration with the California-based biotech firm Amgen, may provide an answer.

Researchers have been testing a novel drug that uses an antibody to block sclerostin, a protein that acts as a natural brake to bone formation. Preventing sclerostin's action allows new bone to be laid down. In July 2011, Bouxsein tested the drug in 15 mice on board the shuttle *Atlantis*. When she compared bone-mass data from these test mice against bone measures from shuttle-based controls as well as Earth-based mice receiving treatment or serving as controls, Bouxsein found that the drug not only helped the test mice maintain bone mass but appeared to induce new bone to form, even in low-gravity environments. If these results hold true in humans, the danger to bone health brought by space travel—or disease—could become a thing of the past.

BRAKE TEST: Space-based experiments designed by Mary Bouxsein found that bone loss in low-gravity environments may be halted, even reversed, by a novel antibody.

FEATHERWEIGHT: During parabolic flights that induce a type of weightlessness, Charles Oman (center) and colleagues investigate the neurovestibular cues that trigger motion sickness.



Shaken and Stirred

When perceptions conflict, motion sickness ensues

Motion sickness is an unforgettable experience for anyone who has ever been afflicted by it. The roiling symptoms can strike while on a boat, in a car, on an airplane, and even while floating weightless in a spacecraft.

Unexpected and unfamiliar motion cues received through vision, the inner ear, and body movement are at the core of the disorder. To get a sense of how closely integrated visual, vestibular, and proprioceptive cues are, try balancing on one foot with your eyes closed.

Charles Oman, an affiliated faculty member of the Harvard–MIT Division of Health Science Technology and director of the Man Vehicle Laboratory at MIT, learned to fly as a teen, developed an interest in air sickness, and, in the late 1970s, began working with NASA to find ways to prevent or lessen the impact of motion sickness among astronauts. Oman proposed that, during deliberate movement, the brain learns what signal pattern to expect from the otoliths and semicircular canals—two of the sensory structures of the inner ear—and cancels these signals out at the brainstem. However, when we unexpectedly stumble or fall, those signals, which affect our sense of balance, remain active and move to the brain's cortical regions where stabilizing reflexes are generated.

Oman hypothesized that this conflict between expected and perceived motion triggers sensory motor learning—and the woe of motion sickness.

These two normal responses—ignoring deliberate movement and stabilizing unexpected motion—are disrupted if signals conflict with the expected patterns. The conflict occurs during weightlessness and other situations where the sensations that the inner ear feels and the sights that the eyes see don't match anything that the brain recognizes as normal motion. Oman hypothesized that this conflict between expected and perceived motion triggers sensory motor learning—and the woe of motion sickness. His theory could explain why drivers rarely get carsick as well as why astronauts get space sick, adapt after several days, and then become sick again when they return to Earth.

Oman notes that a longstanding debate over whether these "sensory conflict" signals exist may now have ended. Using an animal model, researchers recently found brainstem neurons that govern the sensory conflict behavior of the semicircular canal and otolith structures. These neurons are in the reticular formation, a brain area that detects and prioritizes new sensory inputs. The cells are also adjacent to the brain's emetic centers. It appears that when sensory conflict neurons become overloaded, the signal spills into the nearby emetic centers, eventually causing malaise and nausea. Hence the existential bleakness of motion sickness may be a simple evolutionary accident of brain wiring.

Oman often experienced weightlessness and disorientation in parabolic flight: When he floated upside down, the ceiling would suddenly appear to be the floor. Oman realized that this sudden shift in orientation could provoke space sickness. "We told the astronauts, 'Look, if you want to avoid being sick, you and your crew need to all stay visually upright during your first days in orbit,'" Oman says. "'If one of your buddies floats into view and his body is upside down relative to you, that will flip your world upside down. That's a recipe for space sickness.'"

Heart Strings

Decoding signals hidden in a heartbeat

The pulse pounds, breath grows shallow, and blood pressure rises: These are simple physiological responses to excitement or exercise. But as basic as these processes are, they are accompanied by cascades of mechanical, biochemical, and electrical signals. To Richard Cohen '75, this cacophony of data is simply the music of research.

When Cohen entered the inaugural HMS class of the Harvard–MIT Division of Health Science Technology, he had a plan.

"I wanted to analyze and process the second-to-second, minute-to-minute fluctuations in the signals that biological systems generate," says Cohen, a member of the core faculty of HST and the Whitaker Professor in Biomedical Engineering at MIT.

It turned out that NASA and the National Space Biomedical Research Institute were also interested in deciphering those signals: They wanted to determine whether space flight might have long-lasting impact on the cardiovascular health of astronauts.

Cohen began working with NASA, and later, with NSBRI, and eventually developed a tool that characterizes cardiovascular responses by analyzing the relationships between ongoing fluctuations in such physiologic signals as respiration, blood pressure, and heart rate.

Cohen discovered that hidden amid the electrical noise in an ECG trace is a tiny signal that can provide clues about a person's susceptibility to sudden cardiac death, a form of arrhythmia that kills 300,000 people a year in the United States.

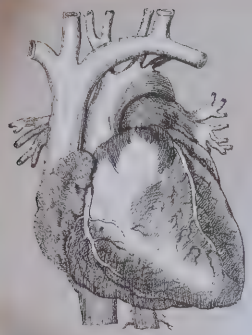
This signal, known as microvolt T-wave alternans, can't be detected by looking at an ECG. It can be extracted only mathematically, using algorithmic filters.

The technology Cohen's team developed is now used as a diagnostic tool to help identify candidates for implantable defibrillators, which can prevent many sudden cardiac deaths.

Cohen has now been listening to the music of physiological data for decades. Even his research is stamped with this interest: One of his first papers was "Beat to beat variability in cardiovascular parameters: Is it noise or music?"

He seems to have found his answer. "Not only is it music," he says. "It's a whole symphony."

Jake Miller is a writer and editor in the HMS Office of Communications and External Relations.



"I wanted to analyze and process the second-to-second, minute-to-minute fluctuations in the signals that biological systems generate."

MAESTRO: Richard Cohen's study of tiny cardiac signals has led to the development of a diagnostic tool that helps identify candidates for implantable defibrillators.

Atmospheric Disturbance

What happens in space, doesn

ways stay in space by R. Alan Leo

ARCTIC-IMAGES/LATITUDE/CORBIS

Valentin Lebedev sensed that something was wrong. ■ "Today passed as usual, but I can feel that I am beginning to get tired and nervous, even though my overall physical condition is good," he wrote. "Tomorrow will be even harder because of its workload."

September 7, 1982, was the cosmonaut's 118th day aboard the *Salyut-7* space station. When completed, his mission would be remarkable for its length—211 days, a record that stood for 13 years—and for the diary that recorded in intimate and unsparing detail his life on the station. The diary recounts not only thousands of research and operational tasks but also Lebedev's frustration with ground control, the grudging silences with his lone crewmate, and his mounting anxiety and depression in the loneliness of space.

Since the dawn of the space age, its architects have recognized the mission-critical importance of human factors—not only nutrition and ergonomics but also management theory and group dynamics. As missions grew in length and complexity, planners devoted more attention to assessing and maintaining the mental health of space explorers, especially as planning for missions to Mars and beyond anticipated ever greater isolation: When an astronaut on Mars asks mission control a question, the reply will follow at least eight minutes of silence.

HELLO DAVE: The quiet beauty of the International Space Station's cupola also carries a sense of isolation, which, when combined with the stresses of close quarters and lengthy missions, can intensify interpersonal conflicts and personal problems.

As technology offers more solutions on Earth and in space, it underscores that the enduring problems are human ones, a conundrum that struck the cosmonaut Lebedev some 30 years ago.

Screen Time

For help with the human factors, NASA has turned to behavioral researchers. Among those is psychiatrist James Cartreine, an HMS instructor in psychiatry in the Program in Behavioral Informatics and eHealth at Brigham and Women's Hospital. He has been exploring how software could be used to deliver behavioral therapy, which applies evidence-based, pragmatic techniques to problems like depression or anxiety. The conversation between behavioral therapist and patient may resemble other psychotherapeutic techniques, but it often follows a series of questions to identify a problem in a person's life and discrete actions to address it. And in those scripts, Cartreine and other researchers saw a way to deliver behavioral therapy without the therapist.

"I wondered how you might automate what a psychologist would do one on one with a patient," says Cartreine, "and it turns out, NASA was interested in how to help astronauts if they developed depression while on a mission."

In 2001, the National Space Biomedical Research Institute gave Cartreine the green light to develop the behavioral therapy software that came to be known as the Virtual Space Station.

Harmonic Convergence

Like its namesake, the Virtual Space Station is an assemblage of modules. Astronaut training modules employ interactive videos to walk users through potential conflicts and strategies to resolve them. One scenario: Your team has made an error that will delay, but not endanger, an experiment. You want to report the cause of the delay to ground control—but your crewmate does not. You can select from a range of responses, from "They'll spend hours trying to figure this out. We've got to tell them.," to "What's wrong with telling ground?," to "Okay, but you're putting me in a bad position.," and the video shows the likely outcomes of your choice, followed by a voice-over discussing the dynamics at play. (Hint: Ultimatums may escalate the situation; questions defuse it.)

Other modules are designed for use during space missions. Self-assessment modules help a user rate personal levels of stress, depression, and interpersonal conflict. Based on a user's responses, the system provides feedback and recommendations. And self-guided treatments help astronauts deal with problems such as depression and conflict, if they arise.

To address depression, which some astronauts have confronted on past missions, Cartreine and his colleagues developed a problem-solving therapy program. As in one-on-one therapy with a counselor, the program doesn't tell users how to solve a personal issue, such as those involving relationships, health, finance, or family. Instead, a series of questions and answers helps the user develop a plan to address it. Follow-up sessions help to gauge progress and, if necessary, to develop a plan B. Throughout the modules, short videos provide background, encouragement, and user-tailored advice on ways to improve problem-solving success. "The goal is to simulate as closely as possible a session with a master therapist," Cartreine says. Although the software has not yet made a trip into space, it has been used in astronaut training.

Anticipating the myriad problems that might crop up during a mission is complicated by the sensitive nature of the data. An astronaut's behavioral health history is part of his or her confidential medical record, which presents a hurdle to researchers. So Cartreine and others have pieced together a picture of the difficulties encountered from news reports, astronauts' memoirs, and other documented accounts, like Lebedev's diary.

Falling Stars

"Today was difficult," Lebedev wrote about crewmate Anatoly Berezovoy on their 60th day in space. "We don't understand what is

going on with us. We silently walk by each other, feeling offended. We have to find some way to make things better."

Other cosmonauts may have had it worse: Evidence suggests that one Russian mission was scrubbed due to depression among personnel and another due to interpersonal conflict.

In the United States, Buzz Aldrin has written candidly about the depression and alcoholism that followed his astronaut career. Former U.S. astronaut Charles Brady committed suicide in 2006, 10 years and two weeks after his only space flight. And in 2007, six months after returning from a shuttle mission to the International Space Station, astronaut Lisa Nowak was charged with the assault and attempted kidnapping of a romantic rival, actions she says were triggered by depression.

Deep Impact

In the wake of Nowak's arrest, NASA administrator Michael Griffin commissioned a review of the space program's mental health care system. The review committee recommended that NASA give more systematic attention to mental and behavioral health issues. But it cautioned that "the use of any behavioral health selection and patient data is a matter of concern for astronauts, family members, and medical and behavioral health personnel."

That concern drove the design of the Virtual Space Station, Cartreine says. Data are stored on a personal flash drive that the astronaut carries—not only during the mission, but also during the years of training. Nothing is transmitted to Earth or stored on shared workstations. The goal is to give astronauts the privacy to work through problems that they feel unable to raise with their flight surgeons. "If astronauts believe that what they say is confidential and that they can answer honestly, we think they will have a better chance of benefiting from the system," Cartreine says.

Another obstacle for researchers has been sample size: There just aren't enough astronauts to generate a large enough volume of data. But this problem is one the space program has confronted and solved by studying what are called analog populations, groups such as Antarctic researchers, crews of underwater research stations, or, in Cartreine's case, firefighters.

"Like astronauts, firefighters live together for days at a time," Cartreine says. "There's this interdependence for safety but also for social support. It's an operational environment, meaning you're working with equipment, as opposed to working in an office. And you can die on the job." Cartreine is working with fire departments in three U.S. cities to test whether a new Virtual Space Station computer program can help these firefighters resolve workplace conflicts.

SOFT TOUCH: James Cartreine has successfully developed software that offers therapy without a therapist.

Cosmic Community

The Virtual Space Station has taken some ribbing. (Comedian Paula Poundstone: therapy is hard when transmissions between Earth and Mars take up to 40 minutes "and the hour only lasts 50.") And Cartreine was amused when a New Zealand TV newsmagazine paired him with David Bowie, whose contribution to the field is the song "Space Oddity." But Cartreine is serious about the potential of computer-based therapy, and has cofounded Cognitive Behavioral Technologies LLC, a company to promote its wide adoption. Cartreine notes that computer-based therapy is being used with wider application overseas, where it has been shown to improve conditions from post-traumatic stress to depression.

The potential benefit is huge: Depression is the leading cause of disability in the United States, and mental health disorders account for four of the ten leading causes of lost productivity. A 2008 study put the annual cost of lost productivity owing to mental health disorders at $198 billion. Behavioral therapy has advanced to the point, Cartreine says, that doctors can be fairly confident that patients who follow protocol will see improvement. And computer-based therapy can deliver treatment that's cost effective and available whenever and wherever it's needed.

As technology offers more solutions on Earth and in space, it underscores that the enduring problems are human ones, a conundrum that struck the cosmonaut Lebedev some 30 years ago. "If you were a construction worker or mechanic, plowing the land or building factories, it would be different," he wrote. "You could turn a blind eye to the imperfections of others. However, in space technology the responsibilities are obviously much more serious, but people are still the same. Social defects cross all borders, and space becomes a mirror of all our terrestrial shortcomings—social, economic, and moral." ■

R. Alan Leo is senior writer and editor in the HMS Office of Communications and External Relations.

ONE SHOE, TWO SHOE: The effects of disrupted sleep patterns or insufficient sleep can affect a person's judgment in matters large and small, such as the choice of which boot matches which foot.

NASA

Blues Cues

Researchers cast a little light on the subject of sleep

by Elizabeth Dougherty

"Dr. Czeisler, Houston has a problem." NASA's mayday came to Charles Czeisler in August 1990, shortly after he had reported in the *New England Journal of Medicine* that he had shifted the circadian clocks of night workers with nothing but a healthy dose of light. ■ In Houston, the space shuttle *Discovery* had been facing repeated delays. Week after week, the astronauts readied for a nighttime launch only to face another deferral. Meanwhile, astronauts were struggling to adjust to the inverted schedule required by the mission's rigid launch window. Sleeping when required, rather than when biologically cued, seemed impossible. NASA administrators told Czeisler they were so desperate for solutions that they were considering a plan to set up a facility overseas, where the astronauts could adjust to a schedule more in sync with what they'd need while on their mission.

Czeisler did not like the sound of this plan. He left for Houston the next day.

Despite the urgency of the situation, NASA decided it needed to launch a decade-long research program before jumping into using light to control the astronauts' sleep–wake cycle. After all, the agency reasoned, Czeisler, the Frank Baldino, Jr., Professor of Sleep Medicine at HMS and chief of the Division of Sleep Medicine at Brigham and Women's Hospital, had reported shifting the clocks of only a dozen or so people.

The only thing that mattered to the astronauts, however, was that Czeisler's light therapy worked. They wanted the lights, and they wanted them now. Based on their flight schedule, Czeisler had two weeks to replicate his laboratory's light-controlled, one-room environment.

When the astronauts finally did launch, they left Czeisler a gift: preflight urine samples that showed they were releasing melatonin, a hormone normally released during periods of darkness, during their night, which was daytime on Earth. The astronauts had successfully inverted their physiological schedules. NASA has since used the lighting treatment for astronauts on any mission that launches at a time requiring a shift of more than three hours from local time.

NASA did carry out a ten-year research program on light therapy, the results of which have led a growing number of astronauts and mission controllers to work with flight surgeons to develop sleep–wake prescriptions tailored to individual schedules. The lessons learned by NASA have the potential to help night-shift workers of all sorts, from police officers and firefighters to hospital workers. The trick, however, has been in translating discoveries from a controlled laboratory environment into a messy world where nurses fit 40-hour weeks into three days but still need to get their kids on the bus every morning, and where almost everyone uses artificial lighting to make each day far too long.

MAGGIE STEBER/NATIONAL GEOGRAPHIC STOCK (ABOVE); KRIS SNIBBE/HARVARD NEWS SERVICE (OPPOSITE)

The Eyes Have It

In Czeisler's early studies of totally blind people, he observed a person without any rod or cone function, the only known light-sensitive cells in the eye, who still responded to light cues by repressing melatonin. It wasn't until 2000 that studies, many funded by the National Space Biomedical Research Institute and carried out by researchers such as Czeisler and Steven Lockley, an HMS associate professor of medicine in BWH's Division of Sleep Medicine, indicated how this was possible.

Studies in animals revealed the presence of melanopsin, a blue-light–sensitive photopigment, in the ganglion cell layer of the eye, which had been thought to be light insensitive. Although few in number, these cells form a light-detecting network across the retina, a web that allows the ganglion cells to react to even indirect light.

The network sends signals to the suprachiasmatic nucleus, a bundle of approximately 50,000 cells, each acting as an individual pacemaker, which nestles in the brain's hypothalamus. This bundle acts as the body's master clock to control circadian rhythms in a number of physiological, metabolic, and behavioral processes.

"This was a new photoreceptor," says Lockley. "People had studied the eye for a long time, and they all had missed it."

Lockley's studies confirmed that this light-sensitive circuit was more responsive

The only thing that mattered to the astronauts, however, was that Czeisler's light therapy worked. They wanted the lights, and they wanted them now.

SLEEPSTAKES: Investigations by Charles Czeisler (on phone, opposite page), Steven Lockley (above), and colleagues in the sleep medicine laboratory at Brigham and Women's Hospital discovered that human circadian rhythms can be reset to normal more effectively when blue light therapy is used, a finding that can aid travelers in jet planes or shuttle craft.

to blue light and that blue light was twice as effective as green at shifting the circadian clock and alerting the brain.

These findings have helped make light therapy more targeted and tolerable. "We now know that just having light in the room can be therapeutically effective," says Lockley. "It doesn't need to be in your face." A recent study from the Netherlands illustrates Lockley's point. Researchers there showed that placing brighter lights in the common areas of care facilities for dementia patients slows the rate of patients' cognitive decline, reduces depression, and delays the onset of functional limitations. With support from NASA and NSBRI, Lockley and others are testing the effectiveness of prototype light fixtures that use blue-enriched white light to alert the body when needed and blue-depleted light to increase sleepiness before slumber.

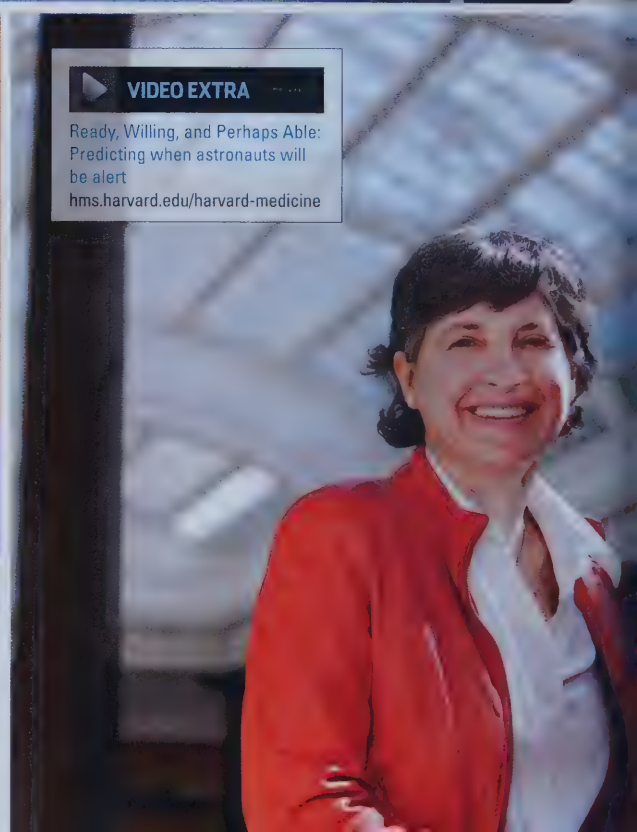
It turns out that lighting technology, too, has matured, offering functionality that can exploit our understanding of the physiological effects of color. A single LED light fixture, for example, can be made to shine blue, green, red, or thousands of different colors or types of white light, at the flip of a switch, allowing alertness and sleepiness to be initiated from one source. "The technology opens new avenues," says Lockley. "We can now consider how to use light in hospitals and other environments that have multiple requirements."

In for the Long Haul

In 1996, when people were walking around Houston wearing "Mars or Bust" buttons, NASA launched the first Mars mission with the rover *Sojourner*.

Each day, *Sojourner* woke with the sun, set into action by its own built-in circadian clock. On Earth, controllers had spent the night calculating where the rover had traveled based on the data it had transmitted before going to sleep. When *Sojourner* woke up, the controllers sent it directions for the day ahead.

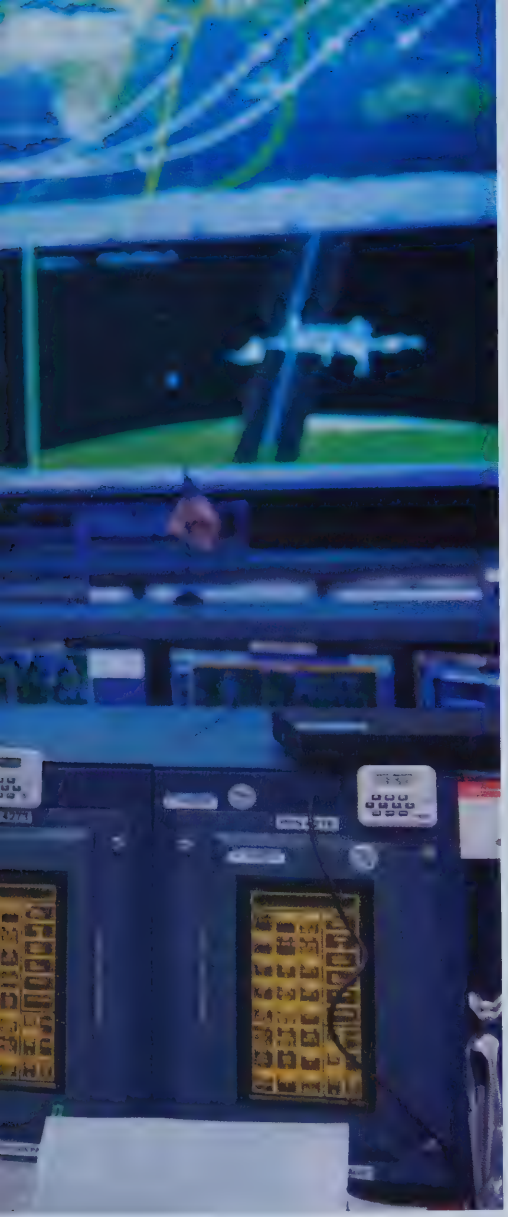
This schedule would have been sustainable for the controllers if not for the fact that a Mars day is 39 minutes longer than an Earth day. "It was like traveling across two time zones every three days. Continuously. For months," says Laura Barger, an HMS instructor in medicine and an associate physiologist in the Division of Sleep Medicine at BWH. Eventually, the Earth-bound crew felt so fatigued they clamored to stop.



VIDEO EXTRA

Ready, Willing, and Perhaps Able: Predicting when astronauts will be alert
hms.harvard.edu/harvard-medicine

ON CALL: Laura Barger (above) found that the hours required of flight control staff can disrupt performance and alertness, condition changes that Elizabeth Klerman seeks to predict using finely designed mathematical models.



Over the years, the mathematical models have evolved into sophisticated software tools that predict how the circadian clock's internal time and rhythm will change with a shift in schedule.

When NASA launched the Mars lander, the *Phoenix*, in 2003, Barger and Lockley teamed up with the controllers to provide a blue-light intervention, the first NASA application of blue-light research. "We were successful at keeping the biological clocks on a Martian day," says Lockley. The results, which show the controllers' melatonin production shifting to match the day length on Mars, are being reviewed.

Vital Signs

Similar research is underway for astronauts on the International Space Station, a space-based research facility. Launched in 1998 and continuously occupied since late 2000, the station is expected to provide a platform for studying how living in space affects human health.

Barger monitored sleep activity among ISS astronauts using actigraphy, a technique that charts sleep–wake cycles by measuring a person's movements with a watch-like device that contains an accelerometer. During sleep cycles, there is less movement.

Barger found that astronauts slept only about six hours per night, far short of the eight hours Czeisler recommends, for example, to professional basketball players to maintain performance. Continuous sleep deprivation has a cumulative effect, so after about a week of short nights, cognitive performance declines in a way similar to that seen with intoxication. Barger hopes that one day every astronaut will wear an actigraph as an operational medical requirement, making sleep measurements a new vital sign for space-based personnel.

That hope may become an easy reality. NASA is so convinced of the importance of restful sleep that, when it upgrades the lighting in the ISS in 2014, it plans to install programmable LED lights that will allow the astronauts to maintain a regular day–night cycle by shifting lights from blue and green to red as the day progresses.

Land of Nod

Throughout the day, alertness waxes and wanes, body temperature and heart rate fluctuate, the body responds differently to medications, and creativity ebbs and flows. "I realized that these cycles would likely affect most biological experiments," says Elizabeth Klerman '86, an HMS associate professor of medicine and associate physician in the Division of Sleep Medicine at BWH. Klerman builds mathematical models of circadian rhythms. "One person's noise," she says, "is another's fascination."

At NASA's request, Klerman and her team continued developing models that predict objective performance and subjective alertness under different work-shift conditions, such as the abrupt schedule changes that occur when a shuttle docks at the space station at off hours. Over the years, the mathematical models have evolved into sophisticated software tools that predict how the circadian clock's internal time and rhythm will change with a shift in schedule. Using data specific to an individual, the software can suggest a schedule of light interventions. It can even predict a person's periods of peak performance and alertness. Such knowledge could help astronauts plan the best ways to prepare themselves to perform complex tasks.

For terrestrial applications, says Klerman, the software could be used by the military to select the most rested pilot for a long-distance mission. And Klerman is discussing with an airline an application that could help commercial pilots assess sleep and safety factors when making their bids for flights. Taking on an extra flight to Hawaii might lose its appeal if a pilot learns she will likely fall asleep midflight.

Power to the Sleepers

In 2001, Czeisler formed the Harvard Work Hours, Health and Safety Group, of which Barger and Lockley are members. The group works with a variety of safety-sensitive professions, such as police officers, firefighters, physicians, airline workers, NASA mission controllers, and most recently, federal air marshals. A major effort of the group centers around designing safer schedules for shift workers.

Klerman, for example, is working with Christopher Landrigan, an HMS associate professor of medicine and an associate physician in the Division of Sleep Medicine at BWH, to apply her software to the design of safer, but still effective, schedules for Children's Hospital Boston, where Landrigan also works in pediatrics.

Two decades have passed since NASA called Czeisler. Today, the use of light and smart scheduling to optimize alertness has become an integral part of NASA missions and operations. Perhaps soon these insights will be tools that help sleep-deprived people on Earth. ■

Elizabeth Dougherty is an author and a freelance science writer based in Massachusetts.

Man in the Moon

The nation's space program got off the ground with th

p of an HMS surgeon

I vividly recall that October morning in 1957. I was a fourth-year student on the surgical service at the Massachusetts General Hospital on rounds with chief resident Jack Burke. To my surprise, he led me, my tired fellow classmates, and a group of equally exhausted but eager surgical residents, to a high balcony of the White Building. There, in the growing light of the new day, a bright speck shone in the sky. A planet, perhaps? A star? No. This celestial traveler, we learned, was *Sputnik*, the first craft launched by humans to travel beyond Earth's atmosphere. Standing there, looking up, we were awed by this amazing feat. But like others at the time, we also were slightly unsettled; the bright spot meant our nation had given ground to the Soviet Union. That flash overhead galvanized the country on a mission to intensify its scientific and engineering efforts. For several of us on that fall day, that challenge felt like both a personal and a national duty. ■ Among young surgeons there is an underlying desire to be the best, to make the dramatic save, and to discover new and revolutionary procedures. Many of us focus our energies on bringing new thinking to the procedures, techniques, and tools of surgery; the number of HMS graduates who have excelled at innovation is legion. One was William Randolph Lovelace II '34. His efforts not only made his name notable on Earth; they also placed it among the stars.

by Anthony Patton

ONE GIANT STEP: William Randolph Lovelace II's contributions to the nation's space efforts have been honored with an unusual memorial: a named moon crater. The Lovelace crater is located on the moon's far side, near its north pole. Joining Earth's natural satellite on this spread is *Sputnik*, crafted by humans (above right).

NASA/JPL/USGS (LEFT); NASA (ABOVE)

PROOF OF CONCEPT: Unable to convince others of the merit of his high-altitude survival apparatus, William Lovelace tested it himself (center, in flight suit). Lovelace's avidity for aviation research later led to his appointment as NASA's first Director of Space Medicine. The appointment ceremony (below) included President Lyndon Johnson (left) as well as Lovelace (center) and members of his family. Lovelace's wife, Mary, is third from the right.

Fledgling Fancy

Lovelace was a pioneer in aviation medicine. The field grew from the need to solve the health concerns of pilots, which burgeoned during World War II as redesigned airplanes allowed combat crews to test new altitudes and speeds. Hypoxia, hypothermia, and the effects of the enormous forces of gravity at high altitudes were among the medical issues flight crews faced. These challenges did not abate with the war's end; instead, they expanded to address those confronting astronauts, our "soldiers of space."

For Lovelace, the chance to bring his knowledge of medicine to bear on aviation-related health problems seemed tailor made. He was born in 1907, a mere four years after the Wright brothers made their historic flights at Kitty Hawk. This was a time when the public's interest in aviation soared, and air shows were popular forms of entertainment, especially around Albuquerque, New Mexico, where Lovelace spent his early years. These spectacular events featured daring pilots doing acrobatics in dangerously flimsy machines. It may have been the excitement of flight, or its challenge, or perhaps its romance that captivated the young Lovelace, but whatever the reason, he developed a passion for flying.

In 1926, at age 19, Lovelace entered Washington University in St. Louis, Missouri, joined the U.S. Naval Reserve Officers Training Corps, and began taking flying lessons. He was still a college student when he won his wings at the Great Lakes Naval Training Station in Illinois, an institution some 300 miles from where he was attending college.

Graduation brought Lovelace face to face with the need to decide upon a career. His decision was eased, however, by a close bond with his namesake and uncle, William Randolph, a highly respected doctor in New Mexico. Lovelace applied and was accepted to HMS. Among those on the faculty at that time were Walter Cannon and, in the School of Public Health, Phillip Drinker, both known for their research on respiration. By design or by fiat, work on respiration was echoed in Lovelace's next accomplishment.

Breathing Space

After commencement, Lovelace began a residency at Bellevue Hospital in New York City. At that time, surgical residencies were usually completed in two years and many of the best candidates chose programs that

In what would be his maiden jump, Lovelace, a BLB mask strapped across his face and an oxygen tank cinched to his leg, leapt into the sky.

offered the greatest amount of operating experience. This made Bellevue, with its large wards of charity patients, a top choice for many. Following his time at Bellevue, Lovelace became a fellow in surgery at the Mayo Clinic. There, no doubt to his delight, Lovelace found a research group dedicated to the study of the physiological effects of high-altitude flight.

Lovelace became deeply involved in this research, and, by 1938, was ready to publish what would become a seminal paper on the effects of high-altitude flight on pilots and crews. In this treatise, the 31-year-old Lovelace described a practical rebreathing mask that could be used by high-altitude aviators. The invention, named the BLB mask after its creators, Walter Boothby, Lovelace, and Arthur Bulbulian, would become a vital piece of equipment for both U.S. and British pilots during aerial battles in World War II.

Wild Blue Yonder

The rumor of another world war was fast becoming fact when Lovelace joined the U.S. Army Air Corps and was named head of the Aeromedical Laboratory at Wright Field in Ohio. There, Lovelace continued his work on respiration at high altitudes.

Although the BLB mask had proven itself to be a life-sustaining piece of equipment during flight, the mask could not save pilots who had to bail out. There was, in fact, no method to provide oxygen during high-altitude drops. Consequently, there were no survivors of parachute jumps from lofty heights. Lovelace applied himself to this problem and developed a light tank that attached easily to an airman's leg and contained what Lovelace calculated would be a supply of oxygen sufficient for survival. Although Lovelace was convinced that this simple device could save lives, others considered it impractical. It remained untested until Lovelace literally took matters into his own hands.

On June 24, 1943, Lovelace convinced a B-17 pilot to take him to 40,200 feet, an altitude that had proved deadly to parachutists. In what would be his maiden jump, Lovelace, a BLB mask strapped across his face and an oxygen tank cinched to his leg, leapt into the sky. Knocked unconscious by G-forces, he awoke in time to guide his nearly disintegrated chute to safety. His only injury: frostbite on a hand that had become gloveless during the fall. Although his commanding officer probably thought a court martial was in order, Lovelace instead was toasted for his discovery and for his courage. The latter earned him the Distinguished Flying Cross for "heroism or extraordinary achievement while participating in an aerial flight."

At war's end, Lovelace was appointed chief of a surgical division at Mayo, and his career seemed settled. Sadly, however, two young sons contracted polio and died.

Grief stricken, Lovelace; his wife, Mary; and their three remaining children returned to Albuquerque, where he joined his uncle's multispecialty clinic. Lovelace's tenure at Mayo, however, had planted the seed of an idea; he convinced his uncle to reformulate the Albuquerque clinic using the Mayo model. The clinic soon grew to become a hospital, linked with the local veterans' hospital, and located near the medical school at the University of New Mexico. Despite his busy life as a surgeon, Lovelace established a new medical research facility, one that spoke to his interest in aviation medicine. The Lovelace Respiratory Research Institute remains a noted center for research on respiratory diseases and on aviation and space medicine.

Moonstruck

In the late 1950s, as it became evident that the Space Age was upon us, the federal government bolstered its already strong support for Lovelace and his clinic by tapping him to become the chairman of the Committee on Life Science at the newly operational NASA.

When the Mercury Project began, it was Lovelace's Institute that conducted rigorous physiological tests on the group of pilots and scientists from which the first cohort of seven U.S. astronauts was selected. Lovelace also pioneered the idea that women should be astronauts; 13 women, in fact, underwent the extensive testing regimen at the Institute and were considered mission ready. Lovelace was encouraged financially in this work by an old friend, Jacqueline Cochran. Known as the First Lady of Flight, Cochran was widely recognized for her aerial achievements, including becoming the first woman to pilot a plane at speeds exceeding that of sound.

President Kennedy's announcement of the moon initiative in 1961 energized NASA and, with new funding from Congress, the agency began work on the Apollo program. Part of that effort involved researching how the human body adapted to low-gravity environments without air pressure or oxygen. In short, how humans would fare in space. The call went out for an experienced physician who excelled in aeronautical medicine. It was answered in 1964, when Lovelace was named NASA's Director of Space Medicine.

Sadly, his appointment was brief. In December 1965, Lovelace and his wife lost their lives in a plane crash near Aspen, Colorado, perishing after the pilot lost his bearings and flew the small craft into the wall of a canyon. Lovelace was 58 years old.

Firmament Fixture

It is not easy to dissect all the factors that make a career successful. For Lovelace, the factors included being a skilled surgeon, a brave aviator, a bold investigator, and an able administrator. Records from those who knew him add that he was a fine gentleman with a great sense of humor.

There are many HMS graduates who became famous surgeons, physicians, or scientists. Hospitals, buildings, and laboratories throughout the world are named for some of these luminaries. But in special tribute to his career and his life's work, Lovelace is the only HMS graduate to be honored with a named moon crater, about as permanent a monument as there can be.

Knowing this, I look up at the full moon with a sense of awe and also a sense of pride, for a bit of HMS shines brightly above. ■

Anthony Patton '58 is a retired thoracic and vascular surgeon whose career was centered at Salem Hospital in Massachusetts.

RAPT AND READY: Schoolchildren at an event at the U.S. Department of Education in Washington D.C. wait for their chance to question astronauts.

PAUL ALERS/NASA

space savers

On Course

Space-based research instills a passion for science in the next generation by Ellen Barlow

The night sky has been called humanity's oldest picture book. Looking upward and outward captures the curiosity that feeds the deepest, and sometimes the most tender, roots of scientific inquiry and discovery. During the *Endeavor* shuttle mission in May 2011, for example, schoolchildren in Tucson, Arizona, peppered astronauts Mark Kelly and Mike Fincke with "chat" questions: How long does it take to get to space? How fast do you travel? What's the strangest thing you've seen in space? ■ NASA's outreach to youth is not new. For decades, agency-funded programs have aimed to instill the thrill of science in the nation's young by collaborating with researchers and teachers on the development of innovative curriculum tools. Joan Reede, dean for diversity and community partnership at HMS, led one such effort, which produced a set of case studies for children in middle and high school. Developed by an interdisciplinary team of scientists and educators, these problem-based case studies have sparked the imagination and curiosity of students in schools throughout the country for more than a decade.

Teacher's Guide

Education is a principal means of community outreach for Reede, part of her quest to increase the diversity of students, trainees, and faculty at HMS. In 2002, Reede, together with HMS professors David Potter, the Robert Winthrop Professor of Neurobiology, and Edwin Furshpan, the Robert Henry Pfeiffer Professor of Neurobiology, each now emeritus, asked whether the case-based method could work in the K–12 classroom. Their answer: a resounding "Yes."

The three teamed up to develop a medical case for middle- and high-school students in the Boston area. Called "Mary's Mystery," the case told the story of a young woman who was taken to the emergency room after she fainted in a park. Included were lessons on the connection between brain injury and seizures as well as activities that helped students think like doctors in order to diagnose Mary's condition.

At the time, problem-based learning had been in use for about seven years at HMS, but it hadn't yet trickled down to the K–12 level. With "Mary's Mystery," however, Reede, Potter, and Furshpan discovered that these sorts of cases appealed to middle- and secondary-school students—and to their teachers.

"The cases have strong science content," explains Reede, "and pique the students' interest in understanding how the content relates to their experiences. The stories encourage the students to realize there is more to know. They open a door rather than close one."

Show and Tell

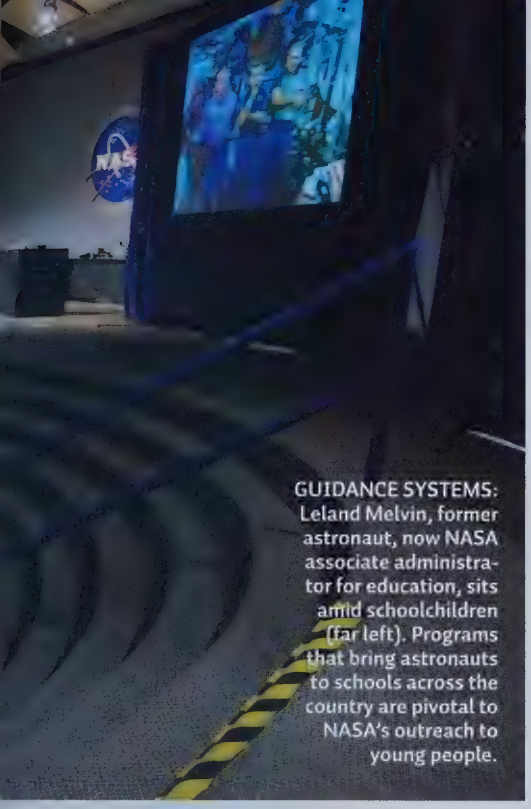
"I still remember the vestibular system," says Justin Owumi, who, as a 14-year-old attended PRISM (Program for Research and Investigation in Science and Math), a hands-on summer workshop at HMS for rising ninth graders. Now a sophomore biochemistry major at Maine's Colby College, Owumi remembers how one of the cases, "Cecilia's Story," grabbed his attention by using participatory demonstrations to illustrate science concepts. Spinning around, for example, helped him understand the role of the inner ear's semicircular canal in maintaining balance, and why dizziness occurs after riding certain amusement park attractions, or, in astronauts, during their first few days in space. "Cecilia's Story," the tale of a woman who developed a balance disorder that caused extreme dizziness and nausea, teaches students about the vestibular system and its role in maintaining balance on Earth and orientation in space.

"I already was interested in science. In fact, my mom and other close relatives always called me 'doctor'," recalls Owumi. "But this program and others I attended at Harvard Medical School catalyzed my love for medicine and science. Now I can't see myself doing anything else."

One challenge for Reede and others who develop science-based educational programs is how to entice teenage boys to enroll. PRISM's success came in part from its partnering with teachers and leaders at community institutions, such as churches, community centers, and YMCAs, to identify and recruit bright students who might benefit.

Aaron Landrum's mother heard about PRISM from someone at her church who knew her son was interested in health care. How did the then 14-year-old feel about being in class during the summer? "That didn't bother me," he says. "It was amazing to be with others like myself who were passionate about science. Plus, it wasn't

NASA (TOP CENTER); JOHN SOARES



GUIDANCE SYSTEMS: Leland Melvin, former astronaut, now NASA associate administrator for education, sits amid schoolchildren (far left). Programs that bring astronauts to schools across the country are pivotal to NASA's outreach to young people.

Reede's team developed the case-based tools to align with national curriculum standards for science education, but the cases also can be modified to comply with various state standards.

like a regular class where you are lectured to for 45 minutes." PRISM students instead would head to the computer lab to research their questions or to the sleep lab to watch a study in progress. From his research experience, Landrum was able to publish a scientific paper that he also presented at some medical conferences.

Now a junior at the University of Pennsylvania, Landrum is traveling through Brazil, Vietnam, and South Africa as part of his study of public health and the social determinants of health, a project for his major in health and societies.

This budding researcher benefited from early encouragement from sources other than PRISM, however. Landrum's parents each have a career in science—his mother is a chemist at the FDA and his father is a therapist and clinical social worker with Boston Public Schools. Even so, Landrum says, it was PRISM that inspired him. "It gave me a strong base of knowledge, opened up opportunities, and empowered me to succeed. To those of us in the program, it offered an environment that showed us we were capable of doing anything."

Good Grades

The success of the team's case-based tools among middle- and secondary-school students came to the attention of Marlene MacLeish, a professor in the Department of Medical Education at Morehouse School of Medicine and a senior education fellow for the National Space Biomedical Research Institute's Education and Public Outreach Program. In 2003, MacLeish offered Reede's team an Institute-funded opportunity to develop problem-based cases in partnership with Morehouse School of Medicine. The collaboration produced "Cecilia's Story" and "What's Up with José?", a case about a high-achieving high-school student whose grades plummeted because he couldn't stay awake in class (it turns out he had a circadian sleep-cycle problem).

NSBRI, overseen by a consortium of 12 universities including Harvard, is funded by NASA to further a dual mission: seek solutions to health concerns facing astronauts on long missions in space, and apply their research advances to benefit health care on Earth. But there is also an unwritten mission, according to MacLeish: "NSBRI wants the knowledge gained through its research to be transferred to students, teachers, and communities."

"Discovery in science is active and dynamic," she adds, "you can't just use didactic approaches to come up with new ideas and approaches." To achieve a similar spirit that would engage and inspire students, "I wanted to start them young with a new way of thinking about problems—asking questions and figuring things out—and I felt that problem-based inquiry was the way to do that."

For Reede, the funding for these cases was an opportunity to build on the curriculum teachers were using with "Mary's Mystery." The cases focused on Earth-based function and dysfunction, but each also included supplementary material for students interested in investigating how the microgravity environment of space affects human physiology. Astronauts can have difficulty sleeping in space, for example, and can feel dizzy or disoriented while adjusting to microgravity.

Classroom Aids

"Cecilia's Story" and "What's Up with José?" are still part of NSBRI's education and training resources, and are available online to anyone interested in exploring their content.

Says Morehouse's MacLeish, "These cases have lasted—and are still being used by teachers across the nation—because educators recognize how easily the cases fit into lesson plans." Reede's team developed the case-based tools to align with national curriculum standards for science education, but the cases also can be modified to comply with various state standards.

Another strength of the tools is the contributions from scientists during their development. In addition to Potter and Furshpan, Charles Czeisler, Baldino Professor of Sleep Medicine at HMS, contributed to "What's Up With José?". Czeisler, who continues to conduct NASA-funded studies, was responsible for developing the sleep–wake schedule guidelines for astronauts and mission-control personnel. Additional expertise for the neurovestibular case came from Charles Oman, an affiliated faculty member of the Harvard–MIT Division of Health Science Technology and director of the Man Vehicle Laboratory at MIT, and Conrad Wall, an HMS professor of otology and laryngology at Massachusetts Eye and Ear Infirmary and director of the MEEI Jenks Vestibular Lab.

Object Lesson

But the ultimate strength of the tools may be found in the young people who, having experienced science through them, are now pursuing health and science careers.

Aaron Landrum plans on graduate training in both medicine and public health. And Justin Owumi admits that since he attended PRISM, "I've dreamed of walking on the HMS Quad as a first-year medical student." All the late nights he now spends studying organic chemistry are easier, he says, because he knows he's working toward that goal.

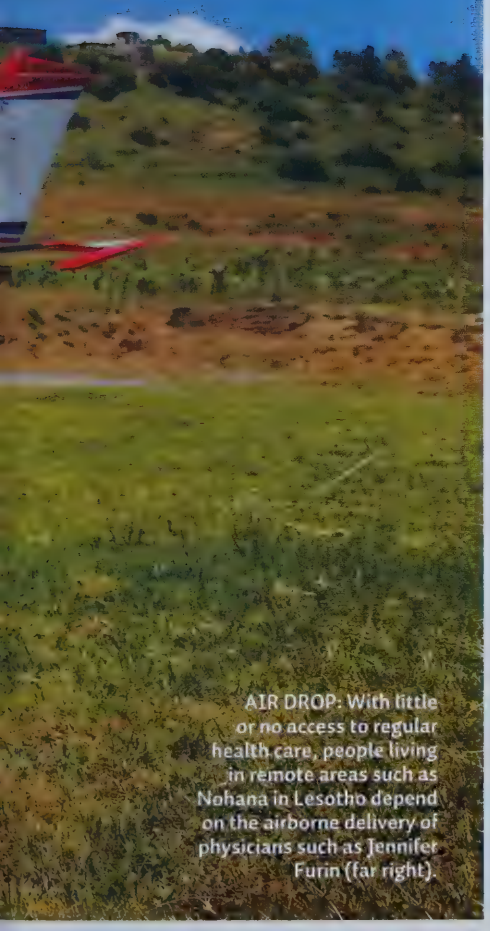
According to Reede, the appeal of space is absolute. "It's the idea that my love of science can take me anywhere," she says, "even into outer space." Or, just as amazingly, to a lifetime of learning the art and science of caring for patients on Earth. ■

Ellen Barlow is a freelance science writer based in Massachusetts.

Medicine takes to the air to serve far-flung population

a wing and a prayer

BY ANGELA ALBERTI

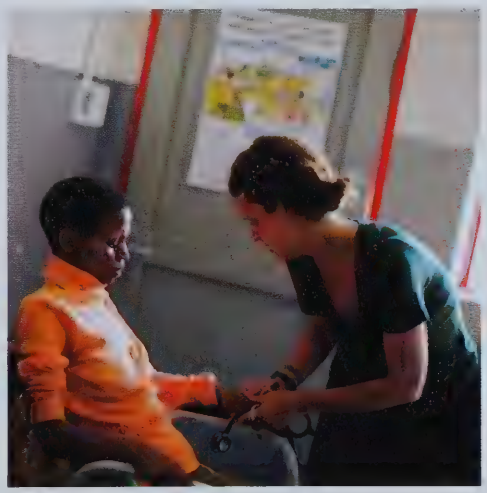


AIR DROP: With little or no access to regular health care, people living in remote areas such as Nohana in Lesotho depend on the airborne delivery of physicians such as Jennifer Furin (far right).

JUSTIN IDE/HARVARD NEWS SERVICE (LEFT AND RIGHT)

CALLED THE MOUNTAIN KINGDOM, Lesotho is the only country in the world situated entirely at elevations above 5,000 feet. It is an enclave, a small island floating within South Africa, its more developed neighbor. Although its rocky perch isolates the nation in many ways, in at least one sense, Lesotho is not alone: Like far too many countries, it struggles to provide its people with access to health care.

"On the day we arrived to survey the clinic site," says Jennifer Furin '99, an HMS assistant professor of medicine, "there were at least 25 people waiting. Yet there was no physician or nurse. So the Ministry of Health doctor and I sat down and began seeing patients. I think at least five people would have died that day had we not been there."



The clinic Furin describes can be reached only by airplane, usually a single-engine Cessna that begins its flight at Moshoeshoe military airfield in Maseru, Lesotho's bustling capital, and ends it an hour later in the mountain village of Nohana. Medical teams that arrive on the unpaved airstrip must carry their bags and crates of supplies on the 20-minute trek to the clinic.

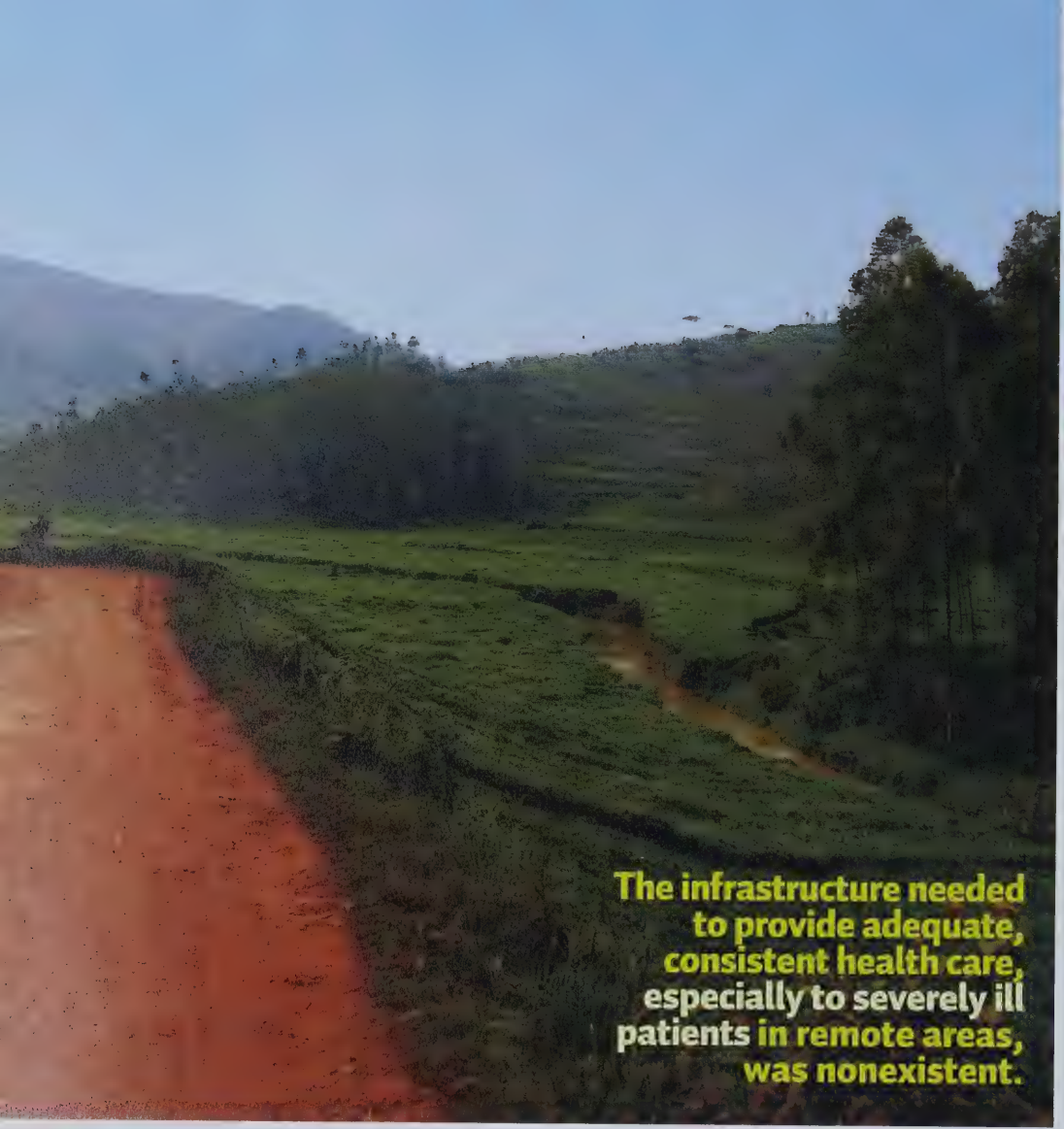
"It's no exaggeration to say the clinics are remote," says Furin, the former medical director for the Partners In Health (PIH) program in Lesotho. "It's like being on another planet. There's no electricity and no cell phone coverage. It's like being transported back in time—not to a good time but to a time when life was very hard."

Rough Terrain

According to a 2006 report by the World Health Organization, a global shortage of 4.3 million health workers has translated into a lack of access to care for more than a billion people. In addition, the UN Millennium Project estimates that 2 billion people, a third of the world's population, lack access to essential medicines. In the poorest parts of Africa and Asia, that proportion climbs to half.

Lesotho is one of 57 countries considered by WHO to have a critical health worker shortage: There are, for instance, only about 80 physicians to care for 2 million people. In addition, nearly one quarter of the population is thought to be positive for HIV, ranking this nation third highest in HIV prevalence globally, according to the U.S. Agency for International Development. And Lesotho's HIV epidemic permeates every corner, rural and urban, of the country. Says Furin, "Shepherds and subsistence farmers living in the countryside have the same rate of HIV infection found among people living in the capital."

Lesotho also has one of the world's highest rates of tuberculosis infection, with a majority of those infected also testing positive for HIV. To complicate matters further, nearly 1,000 people each year contract strains of tuberculosis that are resistant to all first-line drugs.



HOUSE CALLS: Lawrence Shulman (above left) sits with a patient and colleague outside a clinic in Rwanda. Village children gather (right) to look at the images on the mobile phone of a health care worker. Patients visit a clinic in rural Rwanda (far right).

The infrastructure needed to provide adequate, consistent health care, especially to severely ill patients in remote areas, was nonexistent.

Road Trip

Salmaan Keshavjee, a tuberculosis specialist and an assistant professor of social medicine in the School's Department of Global Health and Social Medicine, is no stranger to jumping on a plane to provide care to people in remote settings. "Where I work in Western Siberia," he says, "there are parts of the region that remain unreachable by ground transportation for months each year."

When Keshavjee joined Furin in Lesotho in 2006, the government had already set up seven clinics in isolated parts of the country and had partnered with a nonprofit group of pilots affiliated with Lesotho's health service to deliver supplies to mountain clinics and to airlift the gravely ill to facilities better equipped to care for them. But the infrastructure needed to provide adequate, consistent health care, especially to severely ill patients in the most remote areas, was nonexistent.

Keshavjee found, for example, that the Nohana clinic had no full-time staff, and that there was no capacity for either speedy or sustained care of patients who were infected with HIV and multidrug-resistant tuberculosis.

Pixel Post

Lawrence Shulman '75, chief medical officer and senior vice president for medical affairs at Dana–Farber Cancer Institute, confronted similar difficulties during his travels to provide cancer care to remote populations in Haiti and Rwanda.

"There is little infrastructure in Haiti or Rwanda to provide cancer care," says Shulman. "There are no trained oncologists, and there is little capacity to perform a biopsy. Without a biopsy, processed and read, you can't know a patient's definitive diagnosis. And without that diagnosis, you have no hope of successfully treating a patient."

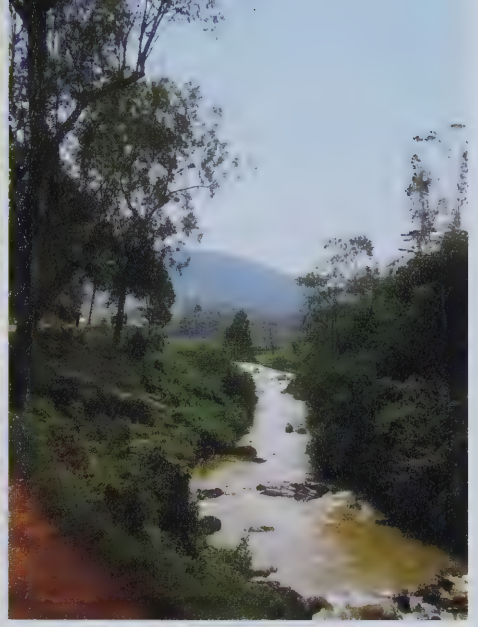
Shulman and colleagues at Dana–Farber, Brigham and Women's Hospital, and Children's Hospital Boston are working with PIH to build cancer care infrastructure in Haiti, Rwanda, and Malawi.

Shulman recently headed up a team of ten Dana–Farber oncologists and oncology nurses that will help run the first national cancer-care training program in Rwanda. The team will share basic knowledge in cancer care and, through remote connections with Boston-based colleagues, will establish ties to improve the delivery of cancer care in that country. Technology is playing a major role in this project, as it does for similar efforts aimed at improving access to health care.

"Paul Farmer, as only he could do, took a picture with his iPhone of a blood smear from a patient with leukemia and sent the picture to me," says Shulman. Farmer '90, the Kolokotrones University Professor of Global Health and Social Medicine, heads the School's Department of Global Health and Social Medicine. "The quality wasn't very good," Shulman adds, "but we were able to make the diagnosis and begin treatment. There are, of course, better ways to do this sort of thing, and we're in the process of trying to figure them out."

Picture Perfect

Keshavjee too is searching for better ways of using technology to deliver care to populations in remote areas. He describes the work of a female colleague in Pakistan who is developing simple strategies to monitor wound infections and other "visible" conditions. She hopes, for instance, to help keep post-operative patients free of infection by monitoring the status of surgical wounds



through photos taken with mobile phones and then shared with wound specialists who help assess the healing process.

"It's very expensive for poor patients to visit a doctor for a surgical wound check," says Keshavjee. "But if you train health workers to take pictures of the wounds and then send those pictures to a doctor, many patients whose wounds are healing well could be saved the expense of a trip. If, however, the wound shows redness or the patient reports pain, the picture could be directed to a surgeon who could decide whether the person should travel to see a doctor."

When faced with basic problems such as how to share medical records with other clinics or with the main office in Maseru, the Lesotho PIH team began using technology creatively. By installing an array of battery-backed solar panels, they provided the clinic with consistent power and communications access without expensive infrastructure, such as the signal transmission towers required by cell phones. They also arranged for access to two small communications satellites, links that allowed personnel in remote clinics to email the main office with requests for medications or supplies. Clinic administrators were also able to communicate better with the patient airlift service to schedule flights or to provide pilots with weather updates. In short, these uses of technology allowed clinic personnel to serve their patients better.


Salmaan Keshavjee

Tech Triage

What does the future hold? Keshavjee thinks the solution to improving access is to develop community-based, decentralized approaches that use technology tailored to help optimize care. And he sees this as a solution for all countries, not only developing nations.

Medical telecommuting would allow experts to consult on questions raised by health care workers traveling within rural or remote populations, says Keshavjee. And those populations could be in mountain clinics, or in inner cities. "In Boston," he notes, "you see many people who are diabetic or who have high blood pressure. Often, they don't see a doctor until they are hospitalized because of stroke or some other emergency."

A combination of community-based health workers and advanced technology would be an alternative to hospital-centric care, one that could achieve better health outcomes, especially for long-term disease management among people living in poor urban and rural areas.

"What if we could give diabetic patients cell phones with an app that allows them to enter their blood sugar values?," asks Keshavjee. "A computer could flag patients whose glucose levels were off, a physician could evaluate those cases and, as needed, have a nurse call or a community health worker visit." This approach, he adds, would not only be more effective, it could also save money by helping people avoid hospital stays and the repercussions of untreated disease.

"How can we link patients with care that can help them?" asks Keshavjee. "We can start by imagining all the ways technology can make distances smaller—and medical care more accessible." ■

Angela Alberti is an editorial specialist in the HMS Office of Communications and External Relations.


express

BY DAVID CAMERON

yourself

NOMENCLATURE IS SERIOUS BUSINESS. Whether you're an expecting parent, a garage rocker immortalizing your latest trio, or an astronomer pondering a mass of orbiting ice, the names you choose symbolize ideals. And so the child's name evokes a poet, the band's provokes convention, and the asteroid, why, it becomes an homage to a Grecian deity. Naming the name arouses a sense of mission.

Now consider this: one-eyed pinhead. Quite a bit of work and life experience went into that particular moniker. It turns out that a graduate student in the lab of geneticist Christiane Nüsslein-Volhard at the University of Tübingen in Germany, had discovered in zebrafish that a particular gene, when mutated, causes a rare developmental disorder in which the embryo fails to divide the eye orbits into two cavities, resulting in a single eye.

Revenge Served Cold

In the world of genetics, when you discover a gene's function, you name it. Consider it a perk. Since zebrafish and fruit fly researchers typically name a gene after the phenotype its mutant spawns, calling it "one-eyed" preserved tradition. This particular student, however, was also going through a nasty breakup with her boyfriend. And so, as an eternal dig to the man who broke her heart, the gene was christened *one-eyed pinhead*.

GREG PARKER

Welcome to the world of gene naming: two parts science, one part acrid wit. Right now, you carry a gene named after a researcher surnamed Harvey (*HRAS*), another named after a retro video game (*sonic hedgehog*), and yet another named after a grad student's dog (*warthog*).

"Most scientists are vain," says Spyros Artavanis-Tsakonas, an HMS professor of cell biology, "and naming things is one manifestation of our vanity. It's how we make our mark, while having some fun!"

But according to Clifford Tabin, the George Jacob and Jacqueline Hazel Leder Professor of Genetics and head of the School's genetics department, such a tradition has practical benefits as well. "These names are visual, and you remember them," he says. "If you name a gene X47326.7, who's going to remember that?"

Not everyone shares Tabin's enthusiasm. The HUGO Gene Nomenclature Committee, which works under the auspices of the Human Genome Organisation, based in Cambridge, England, is determined to scrub the literature of potentially inappropriate names. For HUGO's members, it's a question of acknowledging patients' sensitivities: No one wants to hear that they bear a *warthog* gene. Tabin, in fact, tops the group's most-wanted list of offending namers. In addition to bestowing a fruit fly gene with the name *sonic hedgehog*, his lab is responsible for the *Drosophila* genes *Indian hedgehog*, *desert hedgehog*, *radical fringe*, and *lunatic fringe*—each of which HUGO has directly targeted.

Family Ties

The *hedgehog* genes are part of a larger family of genes involved in embryonic development. In the larvae–maggot stage, fruit flies have bristles on their proto-limbs that aid mobility. The bristles tend to be organized in rows, not unlike bristles on a toothbrush. Genes that affect this bristle patterning were named after spiny mammals, not only the hedgehog but also the armadillo and the porcupine. Other mutations that blocked bristle growth altogether ended up with such handles as *naked* and—borderline creepy—*shaven baby*.

In the early 1990s, Tabin's lab discovered three subtypes of the *hedgehog* genes. Rather than simply cataloging the genes numerically, they decided to name them after different hedgehog species. And so the first was dubbed *desert hedgehog*, and the second *Indian hedgehog*. The researchers had referred to a third subtype as *European hedgehog*. One of Tabin's postdocs, however, had a young daughter who had just been given a *Sonic the Hedgehog* comic book for her birthday. At that time, Sonic the Hedgehog was a character introduced in the eponymous video game developed by the Japanese software giant Sega. The postdoc, who was also a musician on the side, fell in love with the name. So, when the paper was finally submitted, "European" was out, and "sonic" was in.

Could You Repeat That?

Yes, it's that easy. When it comes to claiming your gene, it's less like filing a patent and more like naming a pet. Find a title that's both scientifically and aesthetically pleasing, document it in your published finding, and then, through an unspoken pact, the name gets fixed. Researchers who subsequently stumble upon the same gene in other species maintain the original birth name: What starts in the fly continues to the human. With each published paper, the name becomes more firmly established. If you think this tradition renders HUGO's efforts quixotic, you could be right.

"We always respect the first precedent and stick to the name," says David Van Vactor, an HMS professor of cell biology, who has discovered quite a few fruit fly genes, bestowing them with names such as *stranded*, *shortstop*, *beaten path*, *bypass*, and *walkabout*.

Van Vactor came up with *walkabout* while a postdoctoral researcher at the University of California, Berkeley, working with an Australian scientist. It is a gene whose mutant form causes motor neurons to miss their targets and, hence, to wander at will. Another was identified by a colleague of Van Vactor's who was from the United Kingdom and thus accustomed to the directional miscues of traffic circles. He

ROGUES GALLERY: Although Clifford Tabin (far right to left) and colleagues Spyros Artavanis-Tsakonas, and David Van Vactor celebrate the license given to those who name genes in fruit flies, Gary Ruvkun respects the logic found in the naming conventions used for nematode genes.

named his gene *roundabout*. Yet another gene, one Van Vactor characterized while he was a student, enables membranes in a fly's photoreceptors to form perfect crystalline arrays of microvilli. When mutated, these same arrays descend into chaos, thus, the gene became *chaoptic*.

If you think that sounds like a good name for a rock band, Van Vactor agrees. "I've been struck by the naming of bands over the years," he says, "and I think these mutants provide a lot of grist for that mill."

Toll Story

Yet while names like hedgehog and walkabout are decidedly descriptive, other names are assigned under far more random and serendipitous circumstances.

For example, *Toll* genes, first identified more than 20 years ago, encompass a class of embryogenic molecules that were eventually found to contribute to a fly's immunity to fungal infections. The researcher who first identified the mutant variants of *Toll* was German. Legend has it that when she first observed the mutant phenotypes, she shouted, "Amazing!" But her cry was in German, and, in that language, "amazing" becomes "toll."

Currently, Artavanis-Tsakonas and his lab are examining a particular gene that has revealed some interesting phenotypes. He is pretty sure that the gene will ultimately be named hori. The postdoctoral student leading this research applauds that idea. That postdoc's name? Hori.

A Fly in the Ointment

Things aren't quite so freewheeling in the world of worms, where the nematode *Caenorhabditis elegans* is the predominant model. Nomenclature for worm genes follows more of a card-catalog process. No funny stuff here. All names are based on a classification system inspired by bacterial genetics. Genes that affect lineage, for example, are prefixed by "lin-" followed by a number designating the order of discovery. Currently, *lin* genes number *lin-1* through *lin-66*, and those in between are neither sonic nor shaven.

"The nomenclature for worm genes is really logical," says Gary Ruvkun, an HMS professor of genetics at Massachusetts General Hospital and arguably one of the world's foremost experts on worm genomics, "and quite a disaster for anyone outside of the field. It is a system of mathematical precision but mnemonic catastrophe."

Such systematized taxonomy belies the personality of the father of *C. elegans* genetics, Nobel laureate Sydney Brenner, a man reputed for his wicked sense of humor.

Maybe this is an accident of history. Brenner's research achieved prominence during the 1960s, when computerization was on the rise, and a more orderly and less cheeky approach may have been more fashionable. Compare that with the origins of fruit fly genetics, which can be traced back to Thomas Hunt Morgan's fly room at Columbia University in the early 20th century. In Morgan's era, embryology was all the rage, so that's where all the cool kids went, leaving the "different drummer" types to fly genetics.

"The people who gathered around Morgan were considered pretty weird in their day," says Artavanis-Tsakonas, a proud descendant. "They were very smart, but they were the outcasts. So a certain sociological gestalt developed. That tradition has held for a long time."

But while Ruvkun admits that, as a worm geneticist, he wishes he had such a vehicle for laughs, he cautions that "the fruit fly gene-naming freedom, while memorable, can be disruptive." Examples that immediately come to mind for him are *I'm not dead yet* (abbreviated as *Indy*) and *Ken and Barbie* (describing mutations that remove sex organs).

"In the end," Ruvkun adds, "I think that a naming convention that is not as circumscribed as *C. elegans* and not as self-consciously cute as *Drosophila* would work best."

But the name game has only just begun. While the Human Genome Project has identified roughly 20,000 human genes, many of them have yet to be characterized. And those 20,000 are just genes for protein-coding sequences. DNA codes for a whole lot more than that (microRNAs, anyone?) and so the potential for creativity is as dynamic as ever.

"It's like the dotcom-naming domain," says Van Vactor. "There are quite a few empty slots still out there." ■

David Cameron is the director of science communications in the HMS Office of Communications and External Relations.

F. CARTER SMITH

No Skies, No Limits

TANG. TEFLON. VELCRO. NASA spinoffs? Not a one.

Now try invisible braces, scratch-resistant lenses, ear thermometers, and memory foam. These and thousands of other successful, life-changing products have been developed from research funded and driven by NASA. And to those, add the more than 6,000 inventions and discoveries that the space agency has patented throughout its 50-plus years of innovation and exploration, and you have a small sense of what this massive endeavor has accomplished.

But simply tallying these innovations, or worse, billing NASA as the creator of Tang, misses the point. "It's shortsighted," says orthopedic surgeon and former astronaut Robert Satcher '90. "We should just continue to explore. We cannot possibly anticipate the ideas that will come from that process. And those ideas will certainly revolutionize our lives."

As a modern-day medical case in point, Satcher, now a surgical oncologist at The University of Texas MD Anderson Cancer Center, cites technology he uses daily: magnetic resonance imaging. In the mid-1960s, as NASA ramped up for the Apollo Lunar Landing Mission, engineers at the Jet Propulsion Laboratory at the California Institute of Technology needed to get a better look at the moon's surface. So they devised digital image processing technology. Decades later, scientists applied that same technology to enhance images of the body's internal organs, which eventually made possible the transformative diagnostic uses of MRI scans.

Since Apollo, space exploration has changed, most notably with the launch of the International Space Station. "The ISS is this phenomenal laboratory in orbit that supports a continued human presence in space," says Satcher. "Without it, we wouldn't have a reason—or a way—to ask and answer the kinds of questions we do."

There wouldn't be a reason, for example, to ask what happens to bone and muscle over time in a zero-gravity environment, a key question for astronauts on the anticipated long, zero-gravity journey to Mars. Without any intervention, astronauts lose bone density and muscle mass at a rate of more than 2 percent per month.

During his 2009 voyage into space, Satcher exercised on an antigravity treadmill and resistive exercise device in the space station's gym to help prevent such deterioration. "The downside to that intervention is that you must design a ship large enough to carry the equipment," says Satcher. "So the aim now is to develop drugs or biologically active agents that produce the same results as physical exercise."

Such discoveries translate immediately to clinical medicine. The anti-gravity treadmill, another NASA-based advance, now helps injured patients, such as athletes with joint injuries, recover faster. And certainly, a bone- or muscle-building pharmaceutical agent would be valuable to patients with wasting disorders.

Satcher's voice betrays his excitement over the prospects of a future NASA asteroid mission, followed by a journey to Mars. But the grounding of the shuttle program has temporarily grounded him, too. "I'm too big to fit into a Russian ship, but if the opportunity arises, I'll definitely go into space again," he says. "We'll see what the future holds."

—Elizabeth Dougherty

BACKSTORY

FROM THE COLLECTIONS AT HARVARD MEDICAL SCHOOL

Whether taking the subway to the hospital, flying to a medical conference, journeying by ship to learn from a distant colleague, or driving a team of horses to make a house call, physicians have always traveled for the profession.

Consider the adventurous post-surgery commute of John Brooks Wheeler, Class of 1879. In *Memoirs of a Small-Town Surgeon*, Wheeler describes hopping onto a moving train in East Swanton, Vermont, with two satchels packed with surgical supplies. "I ran at the side...then I grabbed the hand-rails and missed the steps!...It was the nearest that I ever came to being killed and the memory of it is not entirely agreeable."

George Cheever Shattuck, Class of 1905, when addressing an assembly at the McGill University Medical School, described the observations he had made during a world tour. In Hong Kong, he saw "30 odd cases of beriberi"; in the Philippines, he traveled "on a government steamer to collect lepers for segregation in the colony at Culion"; and, Calcutta, he observed, "has much elephantiasis, and the ships bring to it diseases of all sorts from ports throughout the East." —*Susan Karcz*

PHOTO GALLERY

Nineteenth-century watercolor studies of tumor patients in Canton, China
hms.harvard.edu/harvard-medicine

PAUL MORRISON

PERIPATETIC PHYSICIANS: Before there were computer-generated images of the human body and disposable instruments, there were hand-crafted anatomical models, often collected from abroad, and tortoise-handled lancets kept in engraved silver cases that physicians would carry when visiting patients.

The models and instruments shown here include (clockwise, from far left): a Beauchene skull most likely prepared by a French anatomy dealer (mid-nineteenth century); wax models of eyes with ptosis (left), and ectropium, respectively (c. 1875); a pocket medical kit owned by John Collins Warren, first dean of HMS (1816–1817); and a silver *etui* containing two tortoise-shell thumb lancets (c. 1854).

All objects courtesy of the Warren Anatomical Museum at the Countway Library of Medicine.

FIVE QUESTIONS

FOR JACK SZOSTAK

Jack Szostak, Professor, Department of Genetics, Harvard Medical School

Alex Rich Distinguished Investigator, Department of Molecular Biology, Massachusetts General Hospital; Investigator, Howard Hughes Medical Institute; Recipient of the 2009 Nobel Prize in Physiology or Medicine.

What led you to shift from researching telomeres, work for which you received a Nobel Prize, to researching the origins of life?

Our telomere work opened up a lot of questions and brought in many brilliant people who would answer those questions. As this was happening, a lot of new research began coming out about ribozymes and the origins of life. This research caught my interest; I thought my laboratory could make a contribution to this field.

What niche does your lab occupy within the origins-of-life research community?

I see the field as a continuum, from understanding how planets form, to uncovering the early chemistry on a young planet, to the formation of increasingly complex molecules such as amino acids, nucleotides, sugars, and lipids. We're asking, once those building blocks of life were present, how did they get together and start acting like a cell? How did a primitive cell adapt to different environments? How did Darwinian evolution emerge out of this chemistry?

What is your lab working on now?

Pretty much the total focus of our lab is on building a primitive cell. What we want to see in the lab are examples of spontaneous Darwinian evolution. We'd like to discover pathways—a plausible series of steps from simple to more complex molecules, from simple cells to more complicated organisms.

We're working to solve how primitive cells begin to replicate genetic material spontaneously without enzymes. There are a lot of gaps in that story now, but we hope to fill in some of them.

You seem to prefer collaboration over competition. It that true?

It is. I'd rather be in a relaxed environment than in one driven by direct competition. The Harvard Origins of Life Initiative offers me that collaborative environment for it includes scientists from such disciplines as astronomy, earth sciences, chemistry, and biology. It's fun because it's so interdisciplinary. When we talk, we share perspectives that make the research we do together more exciting and, I think, more creative. Several of the astronomers in our group, for example, are involved in the Kepler mission, which is discovering new exoplanets every day. If I talked only with molecular biologists, I would miss opportunities to see beyond my discipline.

What inspired your fascination with scientific inquiry?

My father was an engineer, so I grew up with the idea that you test ideas by building things. That was what my lab did in the telomere story. We built an artificial chromosome to see if it worked the way we expected it to. It didn't. That failure motivated us to learn something new to fill out the story.

We're now taking the same kind of approach to study the origins of life, by trying to build a primitive cell. When we see how things work—or don't work—we ask new questions and discover their answers.

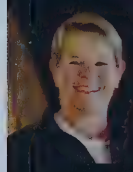
—Susan Karcz

PODCAST

Origins of Life: Nobel Laureate Jack Szostak seeks to build primitive cells
hms.harvard.edu/harvard-medicine

JOHN SOARES

President's Report



The Harvard Medical Alumni Council is fresh from a highly productive winter meeting. On the day preceding the regularly scheduled meeting, we gathered off site to hear David Hirsh describe the HMS Cambridge Integrated Clerkship. According to scores from shelf and board exams, this year-long clerkship appears to better support learning among participating third-year students than the traditional block clerkship approach does. Through an integrated and longitudinal patient-care approach, the CIC fosters scientific, leadership, practice, and professional skills that transcend any medical discipline. The HMS Alumni Council has unanimously voted to recommend pilot longitudinal integrated curriculum experiments in the other major Harvard-affiliated hospitals.

In addition, the Council heard about the tremendous advances in electronic communications that will supplement this exciting magazine, and will be detailed in our upcoming report. We came away with a sense of pride about the advancements at HMS.

Phyllis Gardner '76 is a professor of medicine at Stanford University School of Medicine and a partner at Essex Woodlands.

GARY PARKER (ABOVE LEFT); STEVE GILBERT

HIGH NOTES: Members of the Class of 2015 showed that love can both save the day *and* ensure the future of HMS.

TAKE TWO

Cast of Second Year Show once again saves the HMS day

IN *THE HANGOVERDOSE*, the musical by the Class of 2014, the tradition of lampooning favorite faculty and staff remained alive and well. And, by thwarting an evil genius's diabolic plot, the ensemble assured the School community that it would see a show from the Class of 2015.

The evil genius was none other than Paul Farmer, chair of the Department of Global Health and Social Medicine (portrayed by Will Johnson). In the script by head writers Andrew Le, Matthew Canver, and Samyukta Mullangi, witticisms were lobbed without discrimination, hitting everyone from Dean Jeffrey S. Flier (Nworah Ayogu) to Atrium Café manager Franceny Bedoya (Samyukta Mullangi).

The story opens days before the start of the academic year, when Dean for Medical Education Jules Dienstag (Shaan Ghandi) learns there won't be a Class of 2015. That's because first-year course manager Evan Sanders (Alan Carlotto) is missing after a night of drunken debauchery. Without Sanders, there can be no classes.

Charged with tracking Sanders down, Randall King, the Harry C. McKenzie Associate Professor of Cell Biology (Peter Rozman), recruits a posse made up of Dean for Students Nancy Oriol (Julia Rudolf), Concordia Professor of Pediatrics Joel Hirschhorn (Josh Niska) and Associate Professor Rick Mitchell (Winn Seay).

Director–actors Johnson, Rozman, and Rudolf, together with executive producers Mohammed Karim and Phillip Kim, kept the action brisk. The more than 100 actors, singers, and dancers were accompanied by a 13-piece orchestra conducted by Stephen Allsop. This talented troupe brought the curtain down on Act I with "Don't Stop Achievin'," a *Glee*-inspired tribute to the type A personalities on stage and in the audience.

In Act II, the demoralized heroes retreat to Gordon Hall, where they receive musical encouragement from Associate Professor of Medicine Julian Seifter (David Blauvelt). And the audience heard the night's best solo when Rudolf delivered, "You Make Me Feel Like I'm Hardly a Woman."

After martial arts training at the dojo of Richard Schwartzstein, the Ellen and Melvin Gordon Professor of Medical Education (David Obert), the good guys are ready for action. They recruit reinforcements, including Human Body course co-directors Cynthia McDermott (Carla Heyler) and Trudy Van Houten (Melissa Bellomy), the best comic pair since Laverne and Shirley, and a student army from the dental school led by Bernard Boback and Miguel Ortiz.

Sanders' rescue is timely, allowing him to stop his ladylove, New Pathway course administrator Kristin O'Neil (Megan Koster) from marrying another—the very fear that led to his fateful binge.

—Michael Rafferty

CLASS NOTES

NEWS FROM ALUMNI

1946

John Benson, Jr.
"Retired from the University of Nebraska Medical Center last June and returned to Portland's family and friends."

Milton Hamolsky
"In my third 'retirement,' now serving Home & Hospice Care of Rhode Island."

Theodore Wilson, Jr.
"Living in a Quaker Continuing Care Retirement Community continues to be most pleasant. I am thankful that I am a 12-year survivor of non-Hodgkin's lymphoma."

1947

Clinton Piper
"Diagnosed with bladder cancer in November but have tolerated the therapy well. Spending winters in Palm Springs now with my lovely wife, Patti. Every day is a gift."

Cheves Smythe
"After 41 years at the University of Texas Medical School in Houston, I retired in July 2011. The University conferred an honorary 'near emeritus' degree, and friends and colleagues funded a scholarship for students."

1954

Charlotte Neumann
"Retired but still active with research on nutrition interventions in children and HIV-infected women in Kenya; also writing and working with doctoral students."

1956

John Grover
"Philippa and I are now happily ensconced in our 'honeymoon cottage' at Fredericka Manor in Chula Vista, California. God has been kind to us; for 84 and 82 years of age, we are remarkably well. Enjoying retirement community life, making music, and staying busy."

Russell Rohde
"My love in medicine has been chromosomal genetics and solo cardiology practice. I am indebted to HMS faculty for the studies that fostered research and provided new knowledge, helping to repay that which we were taught."

Richard Sogg
"Playing a lot of music. I continue to serve on the board of the American Beethoven Society, and demonstrate original keyboard instruments at the Ira F. Brilliant Center for Beethoven Studies."

1957

Stephen Friedland
"We enjoyed a cruise along the Columbia, Snake, and Hood Rivers in September with **Arthur** and Iris **McFee**, **Henry** and Deborah **Onken**, **Howard** and Judith **Rubenstein**, and **Richard** and Elizabeth **Wagman**. We're looking forward to this year's reunion."

William Greenough, III
"I continue to work full time running a 41-bed ventilator rehab unit at the Johns Hopkins Bayview Care Center. I chair the endowment committee for the International Centre for Diarrhoeal Disease Research, Bangladesh, and am a trustee of the Child Health Foundation. I hope to see the day when our health care outperforms Cuba's and some other resource-poor countries."

Howard Rubenstein
"Happy to announce that the musical *Romance of the Western Chamber*, book and lyrics by Rubenstein, music by Max Lee, based on the thirteenth-century Chinese classical play *Xi Xiang Ji*, had its premiere at the Grand Dangpo Theatre in Hangzhou, China, on September 9, 2011."

Richard Wagman
"We enjoyed a voyage in the Pacific Northwest with **Arthur**

JOSHUA TOUSTER (THIS SPREAD)

and Iris **McFee**, **Stephen** and Anne **Friedland**, **Henry** and Deborah **Onken**, and **Howard** and Judith **Rubenstein** along the Columbia, Snake, and Hood Rivers. All of us aging nicely!"

1958

Harry Jacob
"Lila and I just celebrated our 58th wedding anniversary. Still teaching, editing a journal, skiing, and golfing."

1959

Boyd Burkhardt
"I retired five years ago at age 72 after a long and successful practice. My wife, Judi, is now receiving care for dementia. The times at HMS were clearly 'days of wine and roses!' "

1960

Mark Perlroth
"I notice that our class notes are moving closer to the front page of the list each year. I continue to enjoy the freedom of retirement but miss the rewards of patient care and teaching."

1964

George Sarosi
"Still working eight months a year as a medicine attending, and it is still fun."

1965

John Mills
"Still enjoying patient care and research in the Antipodes. Many visits to Boston to see daughter **Christina '08**, who is at Children's Hospital Boston, plus her husband Mason and son Alexander."

1966

Scott Nelson
"What a great 45th reunion! I hope everyone will come to our 50th!"

1968

Einar Anderson
"Happily working at Dorn VA Medical Center in Columbia, South Carolina; also conducting the Lake Murray Symphony Orchestra!"

Thomas Pollard
"For the past 18 months I have been busy as dean of the Graduate School of Arts and Sciences at Yale and dean of the faculty for the sciences and social sciences. My lab is still productive, and I continue to enjoy teaching undergraduate cell biology."

1972

Steven Brem
"I was appointed professor and chief of neurosurgical oncology in the Department of Neurosurgery at Penn Medicine, where I will serve as the codirector of the Penn Brain Tumor Center."

Alice Casey
"Still working as a pediatrician in the eastern Sierra Nevada mountains. Now with three grandchildren and a fourth coming soon to a daughter who is a renal pathologist at Columbia. Other daughter is a freelance journalist in Santa Fe, New Mexico. Husband, Cliff, back to work after two joint surgeries."

1979

Andre Churchwell
"I was recently appointed associate dean for diversity at Vanderbilt University School of Medicine."

Nancy Davidson
"Finishing my third year as director of the University of Pittsburgh Cancer Institute and UPMC Cancer Centers. I'm pleased about my recent election to the Institute of Medicine."

1980

Linda Guydon
"I've been selected by my peers as one of Atlanta's top doctors."

Nancy Petersmeyer
"I'm writing from a U.S. Army base in southern Iraq during a six-month deployment as part of a Combat Stress Control Unit. I joined the Army Medical Corps as a psychiatrist at the rank of lieutenant colonel a year ago in a pilot program for experienced physicians. The learning curve has been steep: properly assembling and wearing uniforms, saluting, physical fitness training, a nine-week basic officer leadership course at Fort Sam Houston, a move to the Army's regional medical center in Germany, and now this deployment. Our soldiers are incredibly impressive, and it's an honor to get to

CLASS NOTES

NEWS FROM ALUMNI

JOSHUA TOUSTER

work with them, especially at this stage of my life. If any of you want to learn more about this work, feel free to contact me."

1981

Patricia Cole

"I changed jobs in April, giving up the cath lab and my practice and becoming director of inpatient cardiology at Mercy Hospital in St. Louis—a 1,000-bed hospital—busy, great fun, and NO CALL! Both of our daughters, Elizabeth and Emily, are first-years in medical school. Nice to see the tradition continue!"

Richard Kogan

"I was given the Liebert Award for applied psychoanalysis by the Columbia University Center for Psychoanalytic Training and Research."

John Reilly, Jr.

"I was appointed Jack D. Myers Professor and Chairman of the University of Pittsburgh Department of Medicine."

1982

Aaron Appiah

"Still in private practice of vitreoretinal surgery in Tallahassee, Florida. Hope to attend the 30th reunion."

Hector Picon

"Michelle and I are well on our way to becoming empty nesters. Daughter Michelle Marie is participating in volunteer community work as she prepares to apply to med school, while Monique is completing work in environmental studies and applied biology. That leaves Melissa and Hector Miguel, the next two, to soon leave the nest in pursuit of college studies."

1985

Sheryl Spitzer-Resnick

"Will be married to Jeff 30 years in August 2012. Joshua is 14. I established an independent practice in women's health, integrative medicine, and family medicine in June 2010. Now finding joy in my practice without call or hospital."

1987

Louis Aviles

"Blessed to have one child in grad school, one in college, and the youngest on the way to college. Traveled to Haiti in January to do a medical mission trip."

Donald Budenz

"I am now professor and chairman of the department of ophthalmology at the University of North Carolina School of Medicine."

Timothy Koritz

"I have had the good fortune to be appointed to the Board of Trustees at the University of Illinois. It has been educational and inspiring. The University has the largest medical school in the United States. Unfortunately, I will miss seeing my HMS colleagues at the reunion as we have a Board meeting that conflicts. Best wishes to all in the Class of '87."

1992

Marc Laufgraben

"I have been named head of the Division of Endocrinology, Diabetes, and Metabolism at Cooper University Hospital and associate professor of medicine at Cooper Medical School of Rowan University, both in Camden, New Jersey."

1993

Steven Leon

"Living in Port Jefferson, New York, and practicing neurosurgery with Long Island Neuroscience Specialists with partner Sumeer Sathi '89 since 2001."

1994

Jose Enrique Morales

"Enjoying Northern California with family. Currently Chief of Pediatrics at Kaiser Permanente, Santa Rosa."

2005

Dayle Whiteman-Davenport

"My husband, Milton Davenport III, and I are pleased to announce the birth of our son, Miles Dayton Davenport, on December 2, 2011."

2007

Atul Kamath

"I married my longtime girlfriend, Lauren Meade. We are excited to spend a year at the Mayo Clinic, where I will complete a fellowship in adult hip and knee reconstruction."

OBITUARIES

REMEMBERING DISTINGUISHED LIVES

1940

Frank Sims Moody

Died on December 16, 2011, at the age of 97, after a brief illness, at his home in Mountain Brook, Alabama. Moody served in the Bahamas as a captain in the U.S. Army during World War II. He maintained a private practice in otolaryngology in Birmingham, and was chairman of the Department of Otolaryngology at the University of Alabama School of Medicine from 1953 to 1962. He also helped found the hearing and speech clinic at the UAB Hospital. Moody is survived by June, his wife of 70 years; daughter Louise; and seven grandchildren.

1941

Carl Clinton Gardner, Jr.

Died on September 29, 2011, at the age of 95, in Nashville, Tennessee. Gardner served in the U.S. Army Medical Corps in Africa and Italy during World War II. Gardner began a private practice in Columbia, Tennessee, in 1952. He was a diplomate of the American Board of Internal Medicine and a Fellow of the American College of Physicians. He also was on staff at the former Maury County Hospital until his retirement in 1984. Gardner was predeceased by his wife of 48 years, Clarice. He is survived by his children, Susan, Carol, and David; and three grandchildren.

Curtis Prout

Died on December 2, 2011, at the age of 96, at his home in Manchester, Massachusetts. Prout practiced primary care medicine for nearly 70 years. He joined the faculty of HMS in 1949 and later served as assistant dean for student affairs. He was on staff at Brigham and Women's Hospital from 1947 to 2010. Prout was also the chief of medicine and associate director of Harvard University Health Services from 1961 to 1972. In recognition of his contributions to students and clinicians, the Curtis Prout Academy Fellowship at HMS was established in his honor. Prout is survived by his wife, Diane; his first wife, Daphne; four daughters, Diana Cherot, Daphne Cook, Rosamond Warren, and Phyllis; four stepchildren, Elizabeth Emmons, Catherine Emmons, Robert Emmons III, and Anne Barton; five grandchildren; seven great-grandchildren; and two step-grandchildren.

1942

John Minge Cameron

Died on November 19, 2011, at the age of 93. Cameron served stateside and in India as a physician in the U.S. Army during World War II. In 1949, he started a surgical practice in Montgomery, Alabama, where he later became chief of the Montgomery Surgical Society. He was predeceased by his second wife, Nadia, and third wife, Martha. Cameron is survived by his three children, Chris, Mark, and Jane; and five grandchildren.

1943

Royal Schaaf

Died on October 25, 2011, at the age of 93, of natural causes, in Flemington, New Jersey. Schaaf was medical director at the Prudential Insurance Company until his retirement in 1980. He is survived by his wife of 68 years, Mildred; his children, Kate Martin, Susan Arnone, Virginia Brooks, and Royal; and nine grandchildren. He was predeceased by his granddaughter, Kelly Brooks.

David Stiles

Died on November 21, 2011, at the age of 93, in Damariscotta, Maine. Stiles served as a captain in the U.S. Army Medical Corps. He maintained a private pediatrics practice for 30 years in Irvington, New York. Stiles was predeceased by his wife, Virginia. He is survived by his daughters, Elizabeth Zerner and Joanne Conn; his son, David; two grandchildren; and two great-grandchildren.

Robert Howard Vaughan

Died on December 9, 2011, at the age of 91, at his home in Columbus, Georgia. Vaughan served as a lieutenant in the U.S. Navy in the 1940s, and maintained a private surgical practice in Columbus from 1953 to 1986. He is survived by his wife, Mary; his children, Lea Feinstein, Catherine, Robert, and Thomas; seven grandchildren; and two great-grandchildren.

1944

William Pfeffer, Jr.

Died on September 25, 2011. Pfeffer was one of the first authorities on pediatric exchange transfusions, and, while at Children's Hospital Boston, was among the first to identify maple syrup urine disease. He maintained a private pediatrics practice in Wellesley, Massachusetts, for more than three decades, and was consulting pediatrician to the Parents' and Children's Services of the Children's Mission, now part of the Home for Little Wanderers in Boston. Pfeffer was predeceased by his first wife, Jean. He is survived by his second wife, Angela; son, William; daughter, Jane Jerry; and two grandchildren.

1945

Bennett Young Cowan

Died on December 2, 2011, in Bristol, Tennessee. He served as a captain in the U.S. Army Medical Corps at the VA Medical Center in Johnson City, Tennessee. He maintained a private internal medicine practice in Bristol, Tennessee, for nearly 40 years. Cowan was predeceased by his wife of 64 years, Agnes. He is survived by his children, Bennett, J. Tadlock, Agnes, and Hanson; nine grandchildren; and two great-granddaughters.

Cyrus Rubin

Died on December 19, 2011, at the age of 90, at his home on Mercer Island, Washington. Rubin served as an officer in the U.S. Army Medical Corps. He joined the staff of the University of Washington Department of Medicine as a gastroenterologist in 1954. He developed gastric and intestinal biopsy techniques that led to the accurate diagnosis of celiac disease, and encouraged the food industry to produce gluten-free foods to help these patients. In 1997, the University of Washington School of Medicine honored him with the Cyrus

OBITUARIES

REMEMBERING DISTINGUISHED LIVES

E. Rubin Endowed Chair in Medicine. Rubin is survived by his wife of 64 years, Grace; son, William; daughter, Betsy Deutsch; and five grandchildren.

John Cathro Seed

Died on October 17, 2011, in Princeton, New Jersey. Seed worked at Burroughs Wellcome from 1954 to 1962, developing pain medications and computer models of metabolic homeostasis, and was a researcher in the Department of Anesthesiology at Memorial Sloan–Kettering Cancer Center in New York. Seed was a leader in end-of-life care, and worked at Calvary House, a facility that provided care for terminally ill indigent patients. He ultimately reorganized Calvary House into the Calvary Hospital, which specialized in treating terminal cancers, particularly those of the head and neck. Seed was predeceased by his first wife, Pauline. He is survived by his second wife, Ruth; four children; and seven grandchildren.

1947

Frank Brumback

Died on November 20, 2011, at the age of 89, at his home on Wilson Bay, North Carolina. Brumback served in the U.S. Army as a surgeon, with the rank of captain, during the Korean War. He practiced general surgery in Hagerstown, Maryland, and at the VA Medical Center in Martinsburg, West Virginia. Brumback was predeceased by his first wife, Mary, and by his granddaughter, Margo. He is survived by his second wife, Elisabeth; his son, John; daughters, Mary Lynne Boppe, Barbara Sylvester, and Diana Kershner; one granddaughter; and two great-grandchildren.

Devereux Haigh Lippitt

Died on October 5, 2011. Lippitt served as an apprentice seaman in the U.S. Naval Reserve from 1942 to 1944, and joined the U.S. Army Reserves as a captain in 1950. He served as a pathologist at St. Luke's Hospital in New Bern, North Carolina, from 1960 until his retirement in 1985. Lippitt was predeceased by his wife of 58 years, Gabrielle, and by his son, Peter. He is survived by his children Mark, Anita, Devereux, and Celia; and eight grandchildren.

Robert Wyse

Died on December 7, 2011, at the age of 88, at his home in Morris Township, New Jersey. Wyse served in the U.S. Navy during World War II, and in the U.S. Army at a military hospital in Austria in the 1950s. He had a private internal medicine practice from which he retired in 1993. Wyse was predeceased by his wife, Elizabeth, and by his grandson, Glenn. He is survived by his children, James, Roberta Torres, Heather Emelander, Betsy Jett, and Bruce; and five grandchildren.

1948

Allen Crocker

Died on October 23, 2011, of respiratory failure, in Newton, Massachusetts. Crocker served in the U.S. Army Medical Corps in Nürnberg, Germany, from 1951 to 1953. He retired in 2009 from Children's Hospital Boston, where he was a pioneer in developmental pediatrics. He was also an associate professor of pediatrics at HMS and associate professor of society, human development, and health at the Harvard School of Public Health. Crocker is survived by his wife of 58 years, Margarete; children, Elli Morse, Philip, and Monica Doyon; and nine grandchildren.

John Henry Ohler

Died on December 8, 2011, at the age of 88. Ohler served as a captain in the U.S. Army Medical Corps during World War II and in Korea, and was awarded the Bronze Star. In 1953 Ohler established a medical practice in New London, New Hampshire, and was a member of the staff of New London Hospital until he retired in 1988. Ohler is survived by his wife of 65 years, Priscilla; children, Deborah Hinman, Susan Bliss, Jennifer, Jonathan, Peter, and Rebecca; eight grandchildren; and one great-grandson.

Christopher Southwick

Died on October 25, 2011, at the age of 88. Southwick maintained a private practice with his father in Grand Rapids, Michigan. He was predeceased by his son, Christopher, Jr. Ohler is survived by his wife of 63 years, Charlotte; children, Bill, Suzy Gill, and David; six grandchildren; and seven great-grandchildren.

1949

Dora Goldstein

Died on October 2, 2011, at the age of 89, at her home in Palo Alto, California. Goldstein was a member of the first class at HMS to admit women. She left Bryn Mawr College prior to graduation to conduct chemical research during World War II. Goldstein joined the faculty at Stanford Medical School in 1955, eventually becoming a full professor of molecular pharmacology. An expert on the physiological effects of alcohol, she was the author of *Pharmacology of Alcohol*, widely considered to be the definitive work on the subject. An advocate for women in medicine, she established the Dora B. Goldstein Collection at Stanford Medical School, which archives materials documenting women's contributions there. Goldstein is survived by her husband, **Avram '43**; children Margaret Wallace, Dan, Joshua, and Michael; and five grandchildren.

1950

T. Franklin Williams

Died on November 25, 2011, at the age of 89, of complications of pneumonia, at his home in Rochester, New York. Williams served as a communications officer in the U.S. Navy during World War II. He joined the faculty of the University of North Carolina Medical School in 1956, where he became a professor of medicine and preventive medicine. In 1965, after the passage of the Medicare and Medicaid programs, Williams was invited to organize an interdisciplinary program of services for older uninsured Americans. In 1968, he was named medical director of Monroe Community Hospital in Rochester, New York, and professor of medicine at the University of Rochester School of Medicine

and Dentistry. Williams was director of the National Institute on Aging from 1983 to 1991. Williams was predeceased by his son, Landon. He is survived by his wife of nearly 60 years, Catharine; children, Mary Montague, and Thomas; four grandchildren; and two step-grandchildren.

1951

John Burke

Died on November 2, 2011, at the age of 89, of pancreatic cancer, in Lexington, Massachusetts. Burke served in the U.S. Army Air Force during World War II. Burke worked to improve treatments for severely burned patients, an effort that led him, in the late 1960s, to consult with MIT professor Ioannis Yannas, an expert in polymers and fibers. The team developed a flexible material that protected the burn patient from infection and dehydration and was not rejected by the immune system. Burke was an HMS professor of surgery from 1966 to 1996, and chief of surgery and chief of staff at the Shriners Burns Institute at Massachusetts General Hospital from 1968 to 1980. He became the hospital's chief of trauma services, and helped establish the MGH Burn Research Center. Burke was the Helen Andrus Benedict Professor of Surgery emeritus at HMS, and, in 1991, was honored with the establishment of the School's John F. Burke Professorship of Surgery. He was predeceased by his son, Andrew. Burke is survived by his wife, Agnes; sons, John and Peter, daughter, Ann; and eight grandchildren.

Thomas Eliot Frothingham

Died on December 27, 2011. During the early 1950s, Frothingham served as a medical officer at the U.S. Naval Medical Research unit in Cairo, Egypt. He maintained a private pediatrics practice in Corvallis, Oregon, before becoming a professor of pediatrics at Duke University Medical Center. He founded and was chief of the Division of General Pediatrics at Duke. He helped found the Center for Child and Family Health, a treatment facility for abused and neglected children in North Carolina. Frothingham was predeceased by his former wife, Phyllis. He is survived by their children, Phyllis, Thomas, Benjamin, and David; seven grandchildren; and his former wife, Barbara.

1953

Arthur Goldman

Died on October 3, 2011, at the age of 84. Goldman maintained a private practice in pediatrics, was on staff at Montefiore Hospital in New York, and served as assistant professor of medicine at Albert Einstein College of Medicine. He then served as an associate attending physician at St. Joseph's Hospital, Yonkers General Hospital, and Montefiore Hospital, all in New York. Goldman was predeceased by his daughter, Ilana. He is survived by his wife, Tomiko Ito; and children, Anita Patterson and Sheila.

1954

Arthur Baue

Died on December 28, 2011, in Hamden, Connecticut. Baue served in the U.S. Air Force Reserve from 1955 to 1957, and on active duty as assistant chief of surgery at Clark Air Force Base in the Philippines from 1957 to 1959. He served as a professor of surgery at the University of Pennsylvania School of Medicine from 1963 to 1967, then as surgeon-in-chief and Edison Professor of Surgery at the Jewish Hospital of St. Louis until 1975. Baue moved to Yale University School of Medicine, where he became the Guthrie Professor and chair of the Department of Surgery. He then returned to his hometown to serve as vice-president of St. Louis University Medical Center. Among his many accomplishments, Baue was chief editor of *Archives of Surgery* and director of the American Board of Surgery. In 2008, he received the Lifetime Achievement Award from the Society of Critical Care Medicine. Baue was predeceased by his wife of 55 years, Rosemary. He is survived by his children, Patricia Nizen, Arthur, and William; and seven grandchildren.

Oscar Portman

Died on December 20, 2011, at the age of 87. Portman was a researcher at Harvard School of Public Health and at the Oregon Regional Primate Research Center. He also served as a professor of biochemistry at the University of Oregon Medical School, where he investigated the association between cholesterol and lipoproteins in heart disease. Portman is survived by his wife, Susan; daughter, Margaret Griffey; sons, Richard and Thomas; and one granddaughter.

1956

James Rose

Died on October 3, 2011, at the age of 80. Rose was a commissioned officer in the U.S. Public Health Service, serving for 31 years. He is survived by his wife, Cathie; sons, David, Michael, Jeffrey, Peter, Michael, and Adam; and 13 grandchildren.

1958

Charles Bernard Carpenter

Died on September 30, 2011, in Exeter, New Hampshire, of Alzheimer's disease. Carpenter served as a medical officer in the U.S. Naval Hospital in Yokosuka, Japan. A pioneer in the development of clinical organ transplantation, he served as director of the immunogenetics and transplantation laboratory at Brigham and Women's Hospital, where his career spanned more than four decades. He was a founding member of the American Society of Nephrology, the American Society for Histocompatibility and Immunogenetics, and the American Society of Transplantation. Carpenter is survived by his wife of 55 years, Sandra; sons, Bradford and Scott; and four grandchildren.

1961

William Thomas

Died on November 18, 2011, of cancer. Thomas, an orthopedic surgeon, was a leader in developing total joint replacement techniques. He retired from Brigham and Women's Hospital and the Brigham Orthopedic Association in the late 1990s. Thomas is survived by his wife of 54 years, Margaret; daughters, Annie Williams and Susan Macleod; and four grandchildren.

TAKING A HISTORY

PROFILE OF ROYCE MOSER

FLIGHT DOC: An interest in flying led Royce Moser to undertake the study of respiration at high altitudes and to pursue a career in aerospace medicine.

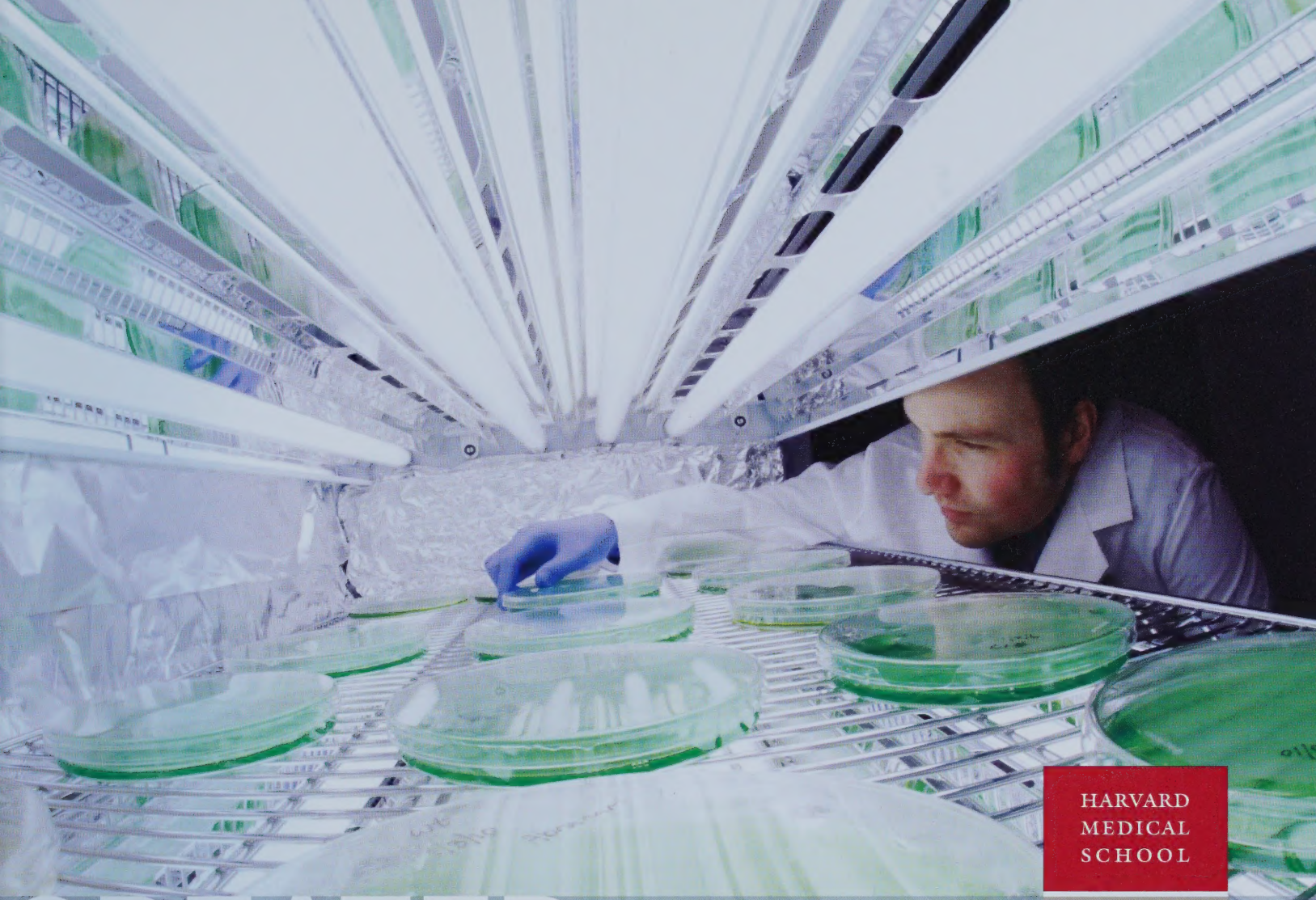
COURTESY OF ROYCE MOSER

CLAIMS TO FAME: Twenty-three-year U.S. Air Force veteran; former commander, USAF School of Aerospace Medicine (USAFSAM); professor emeritus, family and preventive medicine, University of Utah School of Medicine.

FLIGHT PLAN: The high school Royce Moser '61 attended did not offer chemistry, foreign languages, calculus, or physics, yet this valedictorian from Versailles, Missouri, not only graduated summa cum laude from Harvard College, but also earned degrees at the University's medical and public health schools. While at HMS, Moser scoured the literature on respiration at high altitudes, research that grew out of his interest in flying. The search pointed him to Ross McFarland, HSPH's expert in aviation medicine. "McFarland suggested I specialize in aerospace medicine, which I'd never heard of," Moser says. "I did want to fly, but my eyes were too bad to qualify me as a pilot. My other hope was to become a family physician, like my doctors back home." But Moser took McFarland's advice and earned certification in aerospace medicine, family practice, and occupational medicine.

ON THE LEVEL: As a new flight surgeon assigned to a base six weeks before the October 1962 Cuban Missile Crisis, Moser quickly became immersed in supporting the health, safety, and performance of Air Force pilots, other crew members, and their families. Later, during an assignment in Vietnam, Moser worked to prevent and treat physiological and psychological stressors among air crews, including helping them deal with the rigors of hurtling through Earth's atmosphere at supersonic speeds. Crews faced hypoxia; oxygen insufficiency due to plummeting cabin pressures; blackouts, as G-forces pushed blood from the brain to the legs; and spatial disorientation, or "pilot's vertigo," a problem that was of special interest to Moser. In 1969, Moser undertook an analysis of data on disorientation and found that it accounted for 26 percent of fatal Air Force crashes. Although he published this discovery, four decades would pass before the Defense Department used his findings to support installation of automatic ground collision avoidance systems that kick in if an aircraft begins unintentionally nosing toward Earth.

TRAVEL KIT: While heading USAFSAM, Moser oversaw a $61 million budget, much of it slated for research. Advances in medical care developed at the School ranged from oxygen generation equipment that guaranteed pilots stable oxygen concentrations regardless of altitude, to equipment now used to aid patients with chronic obstructive pulmonary disease, to tiny EKG monitors that can diagnose a heart attack in an astronaut in space—or in an Earth-bound patient en route to a hospital. *—Karin Kiewra*



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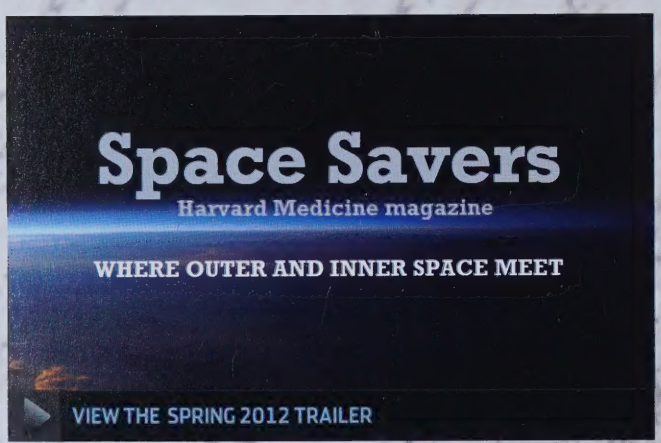

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